THE PROCEEDINGS

of the

Institute of Medicine of Chicago

I

1916-17

CHICAGO

1917

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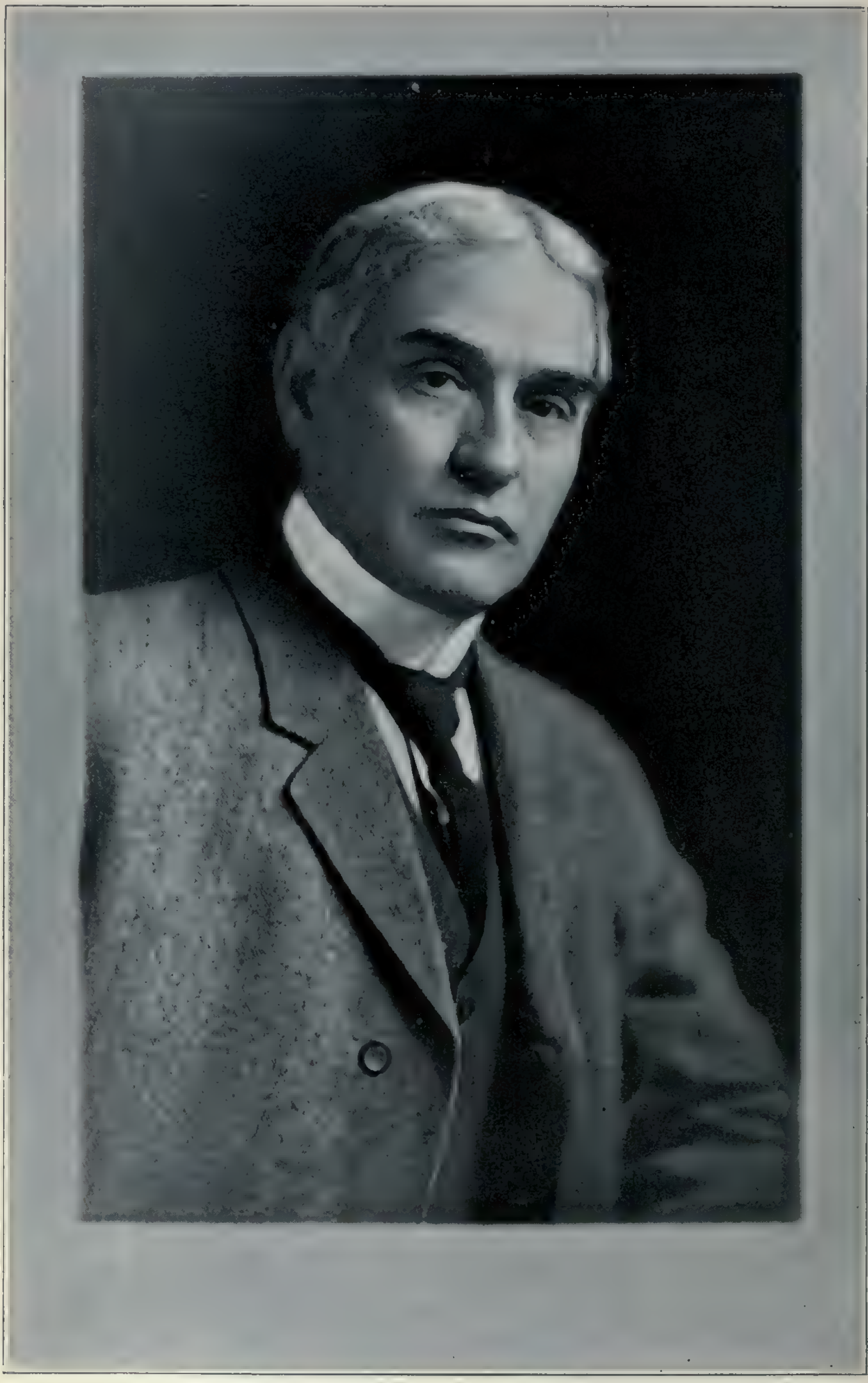

Henry Baird Favill, 1860-1916

HENRY BAIRD FAVILL

1860—1916

Henry Baird Favill was born at Madison, Wis., Aug. 14, 1860. His father was John Favill, a prominent physician of Madison, a man known for his keen powers of observation, his sound judgment, and his hatred of pretense and sham. His mother was a beautiful woman, kindly and gracious, who traced her ancestry on the maternal side to the family of an Indian chief of the Ottawa tribe, Kewinoquot by name.

Dr. Favill's education was obtained in the public schools of Madison, the University of Wisconsin, and Rush Medical College. He received the degree of A.B. from the University of Wisconsin in 1880, when he was less than 20 years of age. This degree at that time implied the classical course, including a study of Greek and Latin. In the fall of 1880 he entered Rush Medical College from which he was graduated with the degree of M.D. in 1883.

Not the least valuable part of his education was received outside the regular curriculum. At Madison his family was one of a cultured, high-minded group, association with which was in itself a liberal education. He profited by taking an active part in college life and in out-of-door sports, especially fishing, hunting, and boating, excellent opportunities for indulging in which were afforded by the lakes and neighboring woods at Madison. To John Bascom, then president of the University of Wisconsin, a man of infectious personality and one of the great moral forces of his time, he owed much in the way of inspiration to high ideals of life and to the service of humanity. In the medical school, too, he had an advantage in that for 2 years he acted as prosector in anatomy, which carried with it the acquiring of special skill from practical work as well as a personal association with the forceful Charles T. Parkes, then professor of anatomy. He also profited by being able to secure several months' service as intern at St. Luke's and Cook County hospitals, Chicago, by supplying the places of interns who were away on vacation or because of illness.

From 1883, the time of his graduation, to 1893 he was engaged in active general practice in Madison, being associated with his father up to the time of the latter's death in 1883. This practice by 1893 had grown to be large and exacting.

June 17, 1885, he married Susan Cleveland Pratt who with a son, John, a graduate of Harvard Medical School in 1914, survives him.

In 1893, largely through the persuasion and advice of medical friends, he moved to Chicago. He located on the North Side. He rapidly became a very busy general practitioner and consultant, his clientele including many of the wealthiest and most aristocratic people of Chicago. Up to the time of his death, while limiting his work to internal medicine, and while doing much in the way of consultation, he remained a general practitioner, a family doctor.

Dr. Favill was a member of many medical societies in several of which he held offices of honor and responsibility. In addition to belonging to societies of a distinctly medical character, he held membership in a number of organizations and clubs of various kinds. He was president of the Municipal Voters League of Chicago and of the City Club.

In Rush Medical College, Dr. Favill was an adjunct professor of medicine from 1894 to 1898; Ingals professor of therapeutics and preventive medicine from 1898 to 1906; and from 1906 to the time of his death professor of clinical medicine offering courses of bedside instruction at St. Luke's Hospital. In this hospital he was for many years an attending physician and at the time of his death was president of the medical staff. He was also on the staff of the Augustana Hospital and the Passavant Hospital. Soon after coming to Chicago he became professor of medicine in the Chicago Polyclinic, retaining this position up to his death.

Dr. Favill on moving to Chicago lived first at 138 Pine Street (February, 1894 to May, 1902), then at 412 East Ontario Street (May, 1902 to May, 1909), finally at 78 East Elm Street (May, 1909 to the time of his death). His office for a time was at his home. In 1898 his office was in the Reliance Building at the southwest corner of State and Washington Streets. In 1902 he moved to the Peoples Gas Building, 122 South Michigan Avenue, having as he had had for some time as office associate, Dr. E. C. Dudley.

While the object of this memorial is to record facts for future reference rather than to express opinion or to place on record a personal estimate on the life of Dr. Favill, a sober word as to his character and influence may be here not out of place.

Dr. Favill was a man of striking appearance; instinctively strangers looked a second time and asked who he was. He was tall, erect, well-

proportioned, carried himself well, and was dignified. "This majestic man" he was called by Rev. Frank W. Gunsaulus who conducted the funeral service. His features showed plainly the mark of Indian ancestry. His love of the open air and the woods, his fondness for walking even in the city where he seldom used a carriage or automobile, his disdain of an overcoat, may have been an outcropping of an inherited trait.

He was a hard worker, beginning his day's task early, finishing late. He was systematic in what he did, punctual in keeping appointments. Whatever inward anxiety and perturbation there might have been did not show on the surface, for he rarely showed irritability or excitement. While not a man given to games, sports, or social pleasures, while in fact pursuing a somewhat independent and solitary course in all he did he was in no sense shut up within himself. While not a mixer in the sense in which the word is now employed, he was loyal to his few intimates, and essentially a friendly man. He was a good companion, a pleasing conversationalist, could be jovial, had a keen sense of humor, and was full of kindly sympathy.

This latter quality may account in a measure for the fact that in the last 10 years of his life he devoted himself more and more to the study and practical solution of questions concerning public welfare rather than questions of individual or local health. He became a leader in efforts made to purify civic life as seen by the active part he took in the affairs of the Municipal Voters League and the City Club, organizations courageously attacking political and social evils. The stand he took in these bodies brought him the antagonism of many men of influence and the loss of patronage of some well-to-do patients. But his alert sense of duty and honor caused him to decide for what he believed to be right even though such action might be attended by some material loss. The same altruistic sentiments together with a broad vision that saw great and distant things led him to participate in local and national crusades against tuberculosis, and to join in work looking to the better understanding of the conditions of mental and social hygiene.

Dr. Favill was a man who conceived and gave birth to big ideas. He was not narrow in his estimate of his profession, in his views of life, or in his life itself. His hold on his people was a strong one. He was not only their physician but in many instances their adviser on matters only remotely connected with health. His clientele was

such that he could have amassed much more in the way of worldly riches than he did. Yet, while showing a shrewd business sense, he was not attracted away from the great things of life by the desire for wealth. He lived a life of principle and service.

As a medical teacher, Dr. Favill was especially happy in the recitation classroom. He had little experience in the conducting of clinics. He was successful as a didactic teacher. Yet he felt that his strength lay in other lines, so in 1906 he deliberately gave up his position as medical lecturer and entered the public civic life to which reference has been made. In his earlier years as writer and speaker he was inclined to use a style that was involved and lengthy, Johnsonian in many respects. Readers and listeners often had difficulty in following his train of thought. Later, whether through conscious effort or not we do not know, he acquired a style, characterized by the same free command of language as before, but marked by a clearness and directness that made him an entertaining and forceful speaker.

Dr. Favill had planned to spend his old age on a farm at Lake Mills near Madison, Wis., a farm that had previously belonged to his family. To this farm he had given thought and study and into it had put considerable money. He had aimed to make it a model dairy farm. His interest in these matters had led to his election as president of the National Dairy Council and Holstein-Friesian Association. Though not feeling well at the time, he started for Springfield, Mass., Feb. 13, 1916, where he was to deliver an address at the annual meeting. He was ill when he reached Springfield, went to the house of George D. Pratt, Mrs. Favill's nephew, and was found to have pneumonia of which he died. His wife and son, John, were with him in his last days. He was attended by Dr. Richard Benner of Springfield and by Dr. F. T. Lord of Boston. It may be of interest to future students to know that the pneumococcus regarded as responsible for his pneumonia was found to belong to Group 1, regarded as comparatively mild; but in spite of this supposedly mild character of the germ and in spite of the use of serum prepared against this group, he succumbed Feb. 20, 1916.

The funeral services were held in the Fourth Presbyterian Church, Chicago, February 22, Dr. Frank W. Gunsaulus of the Peoples Church officiating. No more representative body of people could be collected in Chicago than paid tribute to him on that sad occasion. The burial was at Madison.

Many tributes to Dr. Favill including editorial notices are to be found in the Chicago daily papers published at the time of his death. Medical journals also, for example, The Journal of the American Medical Association, may be consulted for notices of his life. Resolutions will be found on the records of the numerous societies and organizations of which he was a member. A public meeting was held at the City Club Feb. 26, 1916, at which the speakers were as follows: Dr. Frank Billings, Graham Taylor, Sherman C. Kingsley, Frank H. Scott. Allen B. Pond, the president of the club, presided. A copy of The City Club Bulletin for April 28, 1916, is to be found in the records of the Institute of Medicine, which contains the addresses of these men.

This record has been made up by the committee from personal knowledge of facts and acquaintance with Dr. Favill, from a consultation of records of college, hospitals, and societies, and from a reading of notices of his life. Especial help has been obtained from his son, Dr. John Favill who is preparing a memoir that may make this work seem superfluous, and from a memorial[1] written by one who knew him from his Madison days to the end, Dr. John M. Dodson.

NATHAN S. DAVIS,
W. A. PUSEY,
JAMES B. HERRICK,
Committee.

[1] Wisconsin Alumni Magazine, 1916, 17, p. 239.

THEODORE B. SACHS

1868—1916

Theodore B. Sachs was born in Dinaburg, Russia, May 2, 1868, the son of Bernard and Sophie, and was 1 of 5 children. His father was a well-to-do merchant and furnished each of his children excellent educational opportunities.

He was graduated from the high school at Kherson in 1886, and then entered the Imperial University of Odessa as a student of law. While attending this institution he reported for military service and was placed on the reserve list. Following his graduation in 1891, he emigrated to the United States and settled in Chicago.

He pursued the study of English, which he had begun some time before, in the Chicago Athenaeum and at night schools and, concurrently matriculated in the College of Physicians and Surgeons, now the University of Illinois College of Medicine; and although powerful friends were eager to ease his way through life with loans he declined assistance and defrayed his educational and living expenses by working part of the time in the clothing establishment of Hart, Schaffner and Marx. Notwithstanding the handicap of the burden of self-support, he won the faculty medal for excellence in scholarship.

Later in his student career, Sachs became the private secretary of the Imperial Russian commissioner to the Columbian Exposition and, subsequently, served as a clerk and translator in the office of the commission. For a brief period he was also employed in the Chicago Law Institute.

Graduating in medicine in the forefront of his class in 1895, he subsequently served 2 years as an intern in the Michael Reese Hospital, after which he opened an office at the corner of Twelfth and Halsted Streets and engaged in the general practice of his profession. In 1896, he qualified as a citizen of the United States, and on Jan. 4, 1900, he was married to Miss L. Louise Wilson.

While he was yet a hospital intern, Sachs evinced a profound and intelligent interest in tuberculosis and in the unobservant apathy with which the medical profession seemed to regard the unrestrained spread of that desolating disease.

On Dec. 7, 1897, he was elected a member of the Michael Reese

THEODORE B. SACHS, 1868-1916

dispensary staff, and in 1900, he started the first tuberculosis clinic in Chicago in the Jewish Aid Society dispensary. In 1901, he was elected an instructor in medicine in his alma mater, and held this position for 4 years. During the same year he was admitted to the Chicago Medical Society. In 1903, he was appointed by the Cook County Civil Service Commission an attending physician to the Cook County Hospital, but withdrew from this connection at the end of a year of acceptable service.

About this time Sachs began an extensive study of the prevalence of tuberculosis in a densely populated part of the city known as the ghetto district. The investigation was accurate and thorough and covered 3½ years. The results of this study were embodied in a paper read at the meeting of the International Tuberculosis Congress in Washington, D. C., in 1908.

Soon after this he made an extensive study of the "Children of Tuberculous Parents,"[1] covering several hundred families.

During the summer of 1905 he was physician to the Glencoe camp, established by the Visiting Nurse Association, and the pioneer camp in this region for the care of the tuberculous. He was also one of the founders of the Tuberculosis Institute, and during the winter of 1906-1907 attended the patients, about 20, of Camp Norwood, which was established on the grounds of the County Tuberculosis Hospital at Dunning, and maintained by the institute. In 1907, this camp was abandoned, having served the purpose for which it was started, namely, that of proving the practicability of the outdoor treatment of tuberculosis in the vicinity of Chicago. In all this work and many similar undertakings, Sachs was ably assisted by Ethan Allen Gray. It would seem that these activities were enough to consume the time and strength of an ordinary person, but Sachs was able to do much more. In addition to much private work for sick poor, he also found time to serve as the medical director of the Edward Tuberculosis Sanatorium, at Naperville, 1906-1916, and to conduct a successful campaign for the establishment of the Chicago Winfield Tuberculosis Sanatorium at the same time. He served as physician-in-chief of the last institution until Aug. 7, 1912, and following that was head of the consulting staff until his death, April 2, 1916.

In 1912, the board of directors of the National Association for the Study and Prevention of Tuberculosis appointed Sachs chairman of a

[1] Jour. Am. Med. Assn., 1908, 51, p. 1413.

special committee to investigate the present status of hospitals for advanced cases of tuberculosis in this country. The work of the committee is set forth in the proceedings of the association.

Sachs also served as chairman of the committee on labor unions of the National Association for the Study and Prevention of Tuberculosis, and from 1912 until his death he was chairman of the advisory committee of the county tuberculosis institutions.

This committee, consisting of Sachs, Ethan Allen Gray, S. R. Pietrowitz and James Minnick was appointed by the county board. It made a survey of the county tuberculosis institutions at Dunning and Oak Forest, and was directly instrumental in revolutionizing the methods of administration which, for years, had been ignorant and negligent.

At Dunning there was no laboratory and no serious attempt at system in the care of the sick or the preparation and preservation of clinical records.

At Oak Forest the conditions were worse. The committee found 357 patients there and only 1 physician, and only 4 nurses were available for duty at a time. There were no domestic servants. The patients who were able to walk were required to do the police work of the institution.

The recommendations of the committee led to the consolidation of the 2 institutions by the abandonment of the one at Dunning, and physicians and nurses were engaged in consonance with the plan of organization approved by the National Association for the Study and Prevention of Tuberculosis, namely, 1 physician to 50 patients, and 1 nurse to 8 bed-patients. The requisite number of domestic servants was also employed, and a well-equipped laboratory was installed. Patients were not required to do any work except as a therapeutic measure. This plan of administration is in operation at the present time.

In 1909, Sachs was appointed by Mayor William Busse a director of the Municipal Tuberculosis Sanitarium, and he was reappointed to that position by Mayor Carter H. Harrison, June 13, 1912, and again on Nov. 8, 1915, by Mayor William Hale Thompson. He was in charge of the plans of that institution and performed mountains of labor in connection with its construction. He was made president of the board of directors in 1913, and served in that capacity the remainder of his life.

In July, 1911, Sachs organized the factory committee of the Chicago Tuberculosis Institute, the first organization to start a campaign among the great industrial concerns of Chicago and its environs, with a view to safeguarding employees against tuberculosis, and to taking prompt and proper care of those already stricken. This service covers about 250,000 workers. The work of the committee is duly recorded in the archives of the Institute of Medicine.

Sachs also started the Robert Koch Society for the study of tuberculosis. The organization was founded July, 1911, and chartered January, 1915.

The story of the resignation of Sachs from the board of directors of the Municipal Tuberculosis Sanitarium, which he, more than any other person, was instrumental in bringing into existence, is a most depressing chapter in the sordidness, heartlessness, and moral depravity of scheming politicians which the history of Chicago can furnish. The following correspondence merely covers the climax of the movement of politicians to destroy him and to transform the sanitarium into an asylum for hungry and weary henchmen:

CHICAGO, March 20, 1916.

HON. WILLIAM HALE THOMPSON,
Mayor of Chicago.

Dear Sir:

I hereby resign my position as President of the Board of Directors of the Chicago Municipal Tuberculosis Sanitarium. I am taking this step because I do not believe in political management of hospitals, sanitaria, or similar institutions.

My service to the Sanitarium during the past six years has been prompted by the earnest desire to give the best in me to this community in which I have resided during the past twenty-seven years. It is my judgment, after ten months' experience with the present administration, that the continuation of efficient service under the present conditions is absolutely impossible.

Respectfully yours,

(Signed) THEODORE B. SACHS.

March 21, 1916.

DR. THEODORE B. SACHS,
25 East Washington Street,
Chicago.

Dear Sir:

I am writing to acknowledge receipt of your letter of March 20th, tendering your resignation as President and Member of the Board of Directors of the Chicago Municipal Tuberculosis Sanitarium.

Your resignation is accepted.

Yours very truly,

WM. HALE THOMPSON, Mayor.

The death of Theodore B. Sachs by suicide occurred on April 2, 1916.

The tempest of indignation and horror which swept the community as the result of these disclosures and the merciless castigation by the press and by numerous civic organizations, of the mayor and the commissioner of health, John Dill Roberston, for their responsibility in so far as they had been forcing political appointees into the service of the sanitarium and political methods into the administration of its affairs against the earnest protest of Dr. Sachs prompted the guilty officials to declare in public speeches and otherwise that his suicide was really due to the imminence of exposure of an enormous shortage in his accounts — approximating a quarter of a million dollars — and not at all to discouragement and distress resulting from the pernicious political activities of themselves and their satellites. Sachs had been the target of defamatory attacks of various kinds for months before this, of the schemers and moral assassins who were bent on getting him out of their way. But the most searching scrutiny which the experts hired by them could make has failed to discover any spot or stain on the financial record of that gentleman.

We have been permitted to read the farewell letter of Dr. Sachs to his wife and to use it as freely as was found necessary. Extracts from the letter follow:

> . . . I have not much to leave to you except my unsullied name.
>
> There are the $10,000 accumulated in general practice before I began to give my time to the city, the $10,000 insurance and the $3,000 loan to the Edward Sanitarium. This will take care of you and mother. . . .
>
> Please bury me at Naperville, if possible. Services non-sectarian. . . .

In addition to the savings and life insurance alluded to, Dr. Sachs left a balance of $403.20 on a checking account in the Chicago Savings Bank and Trust Company. That is all.

Mrs. Sachs has found it necessary to accept a salaried position in the Edward Sanitarium and holds it now.

That is the answer to the attacks on the character of Theodore B. Sachs.

SACHS — THE MAN

Sachs was a man of uncommon endowments. His mind was not only acute, penetrating and busy, but it was capable far beyond the powers of the commonplace. His professional ideals, his ideals of citizenship, and his standards of character were exalted, clean, and strong. He was almost oppressively serious in nature, and his usual expression was suggestive of sadness and sorrow.

He was utterly lacking in vivacity and sprightliness of nature, and rarely or never exhibited a disposition to playfulness or humor. He spent very little time in laughter.

In the later years of his life he was habitually preoccupied, overwrought, and nervous, and, on occasions, irirtable, brusk, and authoritative in manner. He lacked urbanity and graciousness of nature, and was not adapted to the encouragement of personal attachments. He was not politic, but he was always honest and courageous, and there was never doubt as to where he stood. He was intolerant of inefficiency, negligence, and laziness, even in his closest friends. The friend was ruthlessly brushed aside in the interest of the cause. This was not conducive to personal popularity.

He was not a man of blazing enthusiasms, but he was great with the greatness of things accomplished, and greater still in the lavishness with which he sacrificed his personal interests in order to accomplish them. Chicago can show no better example of unselfish loyalty to a great cause than this.

Sachs may have loved honors and sought them, but he earned every one he received. He was not a seeker for money. Opportunities for the acquisition of large pecuniary gain were pressed on him, and they were calmly brushed aside. Sachs had visions, and they were peopled with the poor and miserable, and with the sick, empty, and despairing of God's creatures. He had a work to do for them, and he did it. It may even be imagined that the manner of his death, although not at all planned for effect, may nevertheless have the effect of greater benefit to the cause than the continuation of his life could have been.

He was an independent thinker and had unusual capacity for initiative and for organization, and his earnestness, his practicality and his wearing industriousness were grandly supported by his transparent disinterestedness. He died gloriously a poor man.

He had great thoughts and plans, greater than the rank and file of his contemporaries could comprehend, and a nature, also, that was far beyound their powers of comprehension.

His work will live for generations yet to come. He was an honor to his profession and a blessing to the community in which he lived and for which he died.

WM. E. QUINE,
FRANK S. JOHNSON,
FRANK CARY,
Committee.

THE PRESENT STATUS OF THE SUPRARENAL PROBLEM

R. G. Hoskins,
January 28, 1916

To formulate a conception of the significance of the suprarenal glands in the existing state of the literature is a somewhat precarious undertaking. The literature, although extensive, is neither consistent nor complete. One can find data that support almost any possible conclusion. One's final conception rests, therefore, to a considerable extent, on the selection and evaluation of more or less conflicting evidence.

From this maze, however, a few important facts stand out unquestioned. Before taking up the present status of the suprarenal problem, in order to afford a background, these facts may be briefly reviewed. Although the suprarenals had long been recognized as definite anatomic structures, the first significant contribution, to our knowledge, of their function was made by Addison, an English clinician. In 1855, he reported that suprarenal deficiency gives rise to a characteristic syndrome the cardinal features of which are muscular weakness, circulatory depression, gastro-intestinal disturbances, and deposition of a dark pigment in the skin and mucous membranes.[1] This discovery constitutes the most important evidence as to suprarenal functioning as we know it today. It also raises the questions that still remain unanswered, namely: What is the specific explanation of this complex? Why does an animal deprived of its suprarenal tissue inevitably die?

The next significant discovery was made by Oliver, another clinician. In an investigation of the effects of various gland extracts on his patients, he discovered that suprarenal material is especially potent. In collaboration with the Edinburgh physiologist, Schaefer, he then undertook an investigation of the properties of suprarenal extracts. It was discovered that such extracts have a remarkable stimulating effect on the circulatory apparatus, causing great augmentation of blood pressure. These observations[2] were published in 1894-1895. The dis-

[1] On the Constitutional and Local Effect of Disease of the Suprarenal Bodies, 1855.
[2] Oliver and Schaefer: Proc. Physiol. Soc., 1894. Jour. Physiol., 1895, 28, p. 230.

covery was made independently by Szymonowicz,[3] however, and published in 1896.

The isolation of the so-called 'active principle'— better an active principle — of the extract was soon after accomplished. Abel[4] in 1897 secured it as a benzoyl-addition product which he called 'epinephrin.' Takamine and Aldrich[5] in 1901 succeeded in isolating it as a pure crystalline substance. They called it 'adrenalin,' which term was adopted as a trade name by the pharmaceutic firm by which they were employed. As a matter of usage, the term 'adrenin' seems now to be generally employed. The substance belongs chemically among the benzene ring compounds, as is indicated by its name dioxyphenyl-ethanol-methyl-amin. Its composition suggests that it may be derived from tyrosin, one of the amino-acids obtained in protein digestion. It is formed in the medulla but not in the cortex of the suprarenal.

The next discovery was made by a group of English investigators, particularly Elliott,[6] whose paper of 1905 has become a classic. He showed that suprarenal extract stimulates selectively the neurocellular endings of the sympathetic nervous system. The effect — at least of physiologic quantities — depends in any organ on three factors: If the organ receives no sympathetic fibers, no effect is produced. If the sympathetic fibers are relatively little used, the effect of adrenin is correspondingly restricted. The effect is either augmentation or depression of the function of a given tissue depending on whether its sympathetic fibers are excitatory or inhibitory. Thus, the uterus is stimulated whereas the intestine is depressed. This discovery seemed to many largely to settle the suprarenal problem. But to this point we shall revert.

Another recent discovery that will probably be recognized as of major importance is that the suprarenals are particularly influenced by emergency conditions. A conception of the 'emergency function' of the glands based largely on work done in his laboratory has recently been formulated by Cannon.[7] Various aspects of this function have been worked out and published in a series of joint papers since 1911. Cannon, in studying the activities of the alimentary tract, had noticed that an outburst of emotion, either fear or anger, resulted in a checking of peristalsis. This might be due to an outflow of impulses through-

[3] Arch. f. d. ges. Physiol., 1896, 66, p. 131.
[4] Abel and Crawford: Bull. Johns Hopkins Hosp., 1897, 8, p. 151.
[5] Am. Jour. Pharm., 1901, 77, p. 523. Am. Jour. Physiol., 1901, 5, p. 457.
[6] Jour. Physiol., 1905, 29, p. 363.
[7] Am. Jour. Physiol., 1914, 33, p. 356.

out the sympathetic nervous system, a phenomenon that is known to occur under such circumstances. However, Cannon was struck by the fact that the depression of peristalsis persisted for some time after all signs of emotion had subsided. Adrenin was known to inhibit peristalsis. The suprarenal glands were known to receive sympathetic fibers and hence supposedly to receive a share of the sympathetic impulses. It was suspected then that the prolonged alimentary depression might be due to an after discharge of adrenin from the excited glands. Direct research confirmed the suspicion.

Cannon in collaboration with de la Pas[8] first studied the effect of violent emotions on the suprarenal content of the blood. The method used was briefly this:

A cat was bound to a comfortable holder. Then under local anesthesia a femoral vein was exposed and opened. This permitted the introduction of a long flexible catheter into the vena cava so as to secure a sample of blood from the level of the suprarenal veins. The animal then had its sensibilities harrowed by the presence of a barking dog. When the anger of the cat was sufficiently aroused, a 2d sample of blood was secured. The 2 samples were immediately compared as to adrenin content. To find a test object that could be used with defibrinated blood was for some time a problem. Finally, however, strips of longitudinal muscle of the cat's intestine were found to be suitable. These immersed in normal blood will undergo spontaneous, long continued, rhythmic contractions. If a trace of adrenin is added, however, the contractions immediately cease. By means of this test the 2 samples of blood were compared. That obtained while the animal was quiet showed no detectable adrenin. That, however, from the excited animal caused a marked depression of the intestinal strip. By suitable means it was shown that the depressing substance actually was derived from the suprarenal glands. It was concluded, therefore, that during times of emotional stress these glands are stimulated to pour into the blood stream enough adrenin to exert a significant influence.

The problem then presented itself: Is this adrenin discharge purely a psychic phenomenon? In other words, could it be produced in an unconscious subject? That problem was investigated by Cannon and Hoskins.[9] Since pain is the most common source of emotion, its effect on the suprarenals was investigated. It was not advisable to subject experimental animals to actual pain, however, hence its physiologic equivalent, sensory stimulation under anesthesia, was employed. A stimulating electrode was adjusted to the sciatic nerve. Then a sample of blood was secured by the method previously described. A strong tetanizing current was applied to the nerve, and after a short period of stimulation, a 2nd sample of blood was secured. Meanwhile it had been found that segments of rabbit intestine are more sensitive and

[8] Am. Jour. Physiol., 1911, 28, p. 64.
[9] Am. Jour. Physiol., 1911, 29, p. 274.

more easily secured than are intestinal strips.[10] In this and subsequent researches, therefore, such segments were used for the tests. It was found, as in the earlier experiments, that blood secured after stimulation of the sciatic nerve gave a clean-cut adrenin reaction. These results have been confirmed by other investigators, notably Elliott,[11] who has observed that sensory irritation results in exhausting the adrenin content of the gland. This fact has an obvious bearing on clinical practice. Any severe surgical operation is essentially a repetition of the experiment described. Suprarenal exhaustion, therefore, is one of the immediate results of such operation. Similarly, it was found that asphyxia causes suprarenal discharge, a fact that has also been confirmed in various ways.

Since this suprarenal discharge may be purely reflex, and since reflexes are usually of direct benefit to the individual, the question arises: Of what use is the arrangement? McDougal has suggested that emotions are the mental representations of bodily activities: anger represents combat, fear represents flight. In case combat results, pain is experienced. Either flight or combat causes partial asphyxia, that is, breathlessness, at least until the body has had time to adjust itself to the conditions. All such activities cause suprarenal discharge. This discharge might be supposed, therefore, to aid in some way in strenuous muscular activity, that is, to integrate the body for muscular response to the stressful condition which caused the discharge.

As a matter of fact, the injection of adrenin does have a number of effects that aid in violent muscular activity. A quiescence of the whole digestive system results and the blood is shifted from the splanchnic circulation to the active muscles, and to the nervous and respiratory organs. The circulation in these organs is further increased by a rise of blood pressure resulting from vasoconstriction of the splanchnic area and often of the skin, as well as by augmented cardiac discharge. In a direct investigation, Hartman,[12] working in Cannon's laboratory has recently shown that a given dose of adrenin simultaneously dilates the vessels of the muscles and constricts those of the splanchnic organs. A discharge of dextrose occurs, leading to hyperglycemia, whereby the laboring muscles obtain a better supply of energy material. This hyperglycemia has been observed as a direct result of strong emotion as well as of artificially augmented adrenin. The well-known bronchodilator

[10] Hoskins: Jour. Pharmacol. and Exper. Therap., 1911, 3, p. 93.
[11] Jour. Physiol., 1912, 44, p. 374.
[12] Am. Jour. Physiol., 1915, 38, p. 438.

effect of adrenin is of use in aiding free breathing, whereby the oxygen necessary to violent activity is secured. Most striking of all, however, the laboring muscle itself is directly benefited. Cannon and Nice[13] observed that after the injection of adrenin or stimulation of the splanchnic nerves to cause suprarenal discharge, the efficiency of a fatigued muscle is improved, sometimes 100 per cent. Gruber[14] has found that recovery from fatigue is greatly hastened by the injection of adrenin. The explanation of this fact is not definitely known, but a hint is offered by Evans and Ogawa,[15] who observed that in the heart at least the assimilation of oxygen is increased by this substance. Hartman's observation that adrenin has a selective vasodilator influence in muscle also comes to mind. Cannon, Gray, and Mendenhall[16] have noted another phenomenon which is of further use in case the stressful condition results in bodily injury: Adrenin lessens the coagulation time of the blood. This is true, however, only within physiologic limits — for such quantities as can be obtained by stimulating the splanchnic nerves. In case greater quantities are employed, the coagulation is interfered with. With regard to this fact, adrenin might well come into frequent clinical use in combating hemorrhage. Cannon suggests that the pains of labor are of direct use to the mother in causing suprarenal discharge and thereby protecting her from postpartum hemorrhage. One thinks also of the stimulating effect of adrenin on the uterus. It seems to be established that in times of stress the suprarenal glands are stimulated to discharge a secretion that is of use in integrating the body to cope with emergencies.

The question may now be raised: What part do the suprarenals play during periods of more placid existence? A few years ago a satisfactory theory could be constructed as follows: An animal deprived of the suprarenal glands dies. The blood pressure falls, indicating that the sympathetic nervous system has failed in its function. Injection of suprarenal extract causes a marked rise of pressure; therefore, the function of the suprarenal glands is to maintain the tonus of the sympathetic nervous system. This might be designated the 'tonus theory.' Although several facts are in contradiction to it, the theory still has considerable currency.[17]

[13] Am. Jour. Physiol., 1913, 32, p. 44.
[14] Ibid., 1914, 33, p. 355; ibid., 1913, 34, p. 89.
[15] Jour. Physiol., 1914, 47, p. 446.
[16] Am. Jour. Physiol., 1914, 34, pp. 225, 232, 243.
[17] Biedl: Innere Sekretion, 1913, I Teil, s. 39.

The first question that arises when one considers the theory is this: Is there present in the blood stream as it leaves the heart enough adrenin to exert any appreciable influence on the sympathetic nervous system? Various statements in the earlier literature occur which indicate that the blood does contain considerable quantities. The concentration is given as, for example, 1 : 10,000,000. But it is interesting to note that as the technic of such determinations has improved, the dilution of adrenin has continuously approached infinity. The best method now known for such tests is to run the suspected blood through the capillary bed of a frog's legs and note the rate of outflow. Trendelenburg,[18] the recognized authority on this method, has recently reported that the concentration of adrenin in arterial blood is at most not more than 1 part in 1 or 2 billions, or only one-fifth enough to exert any appreciable effect on the sympathetic system of a mammal.

The tonus theory can be considered from another point of view. It assumes that the suprarenals are constantly supplying enough secretion to stimulate the pressor mechanisms. This being true, the addition of a little more of the drug by vein should augment this pressor influence and send the tension higher. As a matter of fact, quite the opposite occurs. Such injections characteristically lower the pressure. This observation was made by earlier investigators, notably by Moore and Purinton,[19] but was ascribed to impurities in the material used. In 1912, Hoskins and McClure[20] reinvestigated the matter, using a supposedly pure drug. Their experiments were made on dogs. The depressor effect was easily demonstrated. The fact was confirmed for cats by Cannon and Lyman.[21] In 1913, Hoskins and McPeek[22] showed that light massage of the suprarenals leads to a similar fall of pressure.

If the suprarenals are pouring into the blood stream enough secretion to hold up pressure, sudden occlusion of the suprarenal veins should cause a prompt fall of pressure. Such procedure leaves the pressure exactly where it was before.[23] It is a matter of hours before a fall occurs, whereas circulating adrenin is destroyed within 1 or 2 minutes.

Hoskins and McClure[24] have tested the theory in another way. If adrenin is injected into a vein at small but gradually increasing rates,

[18] Arch. f. exper. Path. u. Pharmakol., 1915, 69, p. 154.
[19] Arch. f. d. ges. Physiol, 1900, 71, p. 483.
[20] Arch. Int. Med., 1912, 10, p. 353.
[21] Am. Jour. Physiol., 1913, 31, p. 373.
[22] Jour. Am. Med. Assn., 1913, 60, p. 1777.
[23] Kahn: Arch. f. d. ges. Physiol., 1911, 140, p. 286. Hoskins and McClure: Am. Jour. Physiol., 1912, 30, p. 192. Trendelenberg: Ztschr. f. Biol., 1914, 63, p. 155.
[24] Am. Jour. Physiol., 1912, 31, p. 59.

at first no effect is to be seen. Then various changes occur. One of the earliest is depression of intestinal peristalsis. If simultaneous tracings of peristalsis and blood pressure are taken, it is found that the intestine is paralyzed before any rise of blood pressure occurs. One need not point out the futility of an arrangement that could maintain blood pressure only at the expense of gastro-intestinal paralysis. Attractive as the tonus theory was, it is no longer tenable.

But suprarenal extirpation is fatal and the final symptoms include a failure of functions that are under sympathetic control. Elliott[25] has offered the suggestion that a minute quantity of circulating adrenin is necessary, not to stimulate the sympathetic system, but to maintain its irritability. That is, the terminal neurocellular substance of the sympathetic system in the absence of adrenin is no longer able to transmit impulses. This possibility also was investigated in our laboratory. It seemed to us that no significant information could be gained from experiments on animals at the point of death, such as Elliott worked on. Various secondary factors may enter into the experiment. If sympathetic failure is characteritic of the syndrome, it should appear at an early stage. It was found that at a time when the animal deprived of the suprarenals is showing marked evidence of that fact — when it can scarcely sustain its own weight, its vasomotor system responds to stimulation perfectly.[26] Vasomotor, that is, sympathetic failure, therefore, is to be regarded as a secondary feature. Both muscular and cardiac weakness precede it.

It would seem probable that if a trace of adrenin is essential for sympathetic functioning, the vasomotor reactions should be improved if an animal previously deprived of the suprarenals were to receive a continuous injection of very dilute adrenin for half an hour. In carrying out this experiment, it was noted that such injections often actually impede sympathetic functioning. In some cases pronounced block was demonstrated.[27] This observation, which was confirmed many times both in normal animals and those deprived of the suprarenals, seems to dispose of the alternative theory that adrenin facilitates sympathetic functioning. In then follows that the remarkable effect of larger doses of adrenin on the sympathetic system is of use in emergencies only.

The possibility still remains that minute quantities of adrenin are necessary for the metabolism of other tissues, for example, as Crile[28]

[25] Jour. Physiol., 1904, 31, p. 20.
[26] Hoskins and Wheelon: Am. Jour. Physiol., 1914, 34, p. 172.
[27] Hoskins and Rowley: Ibid., 1915, 37, p. 471.
[28] Jour. Am. Med. Assn., 1915, 65, p. 2129.

supposes, the brain cells. If such were the case, if adrenin failure were the significant feature in suprarenal deficiency, it should be possible by continuous injections of adrenin to preserve the life of the animal operated on. But no significant prolongation of life can thus be achieved.[29] Laying all theories aside and facing this fact, one can scarcely escape the conclusion that adrenin has no essential connection with the Addison syndrome or its laboratory equivalent, that it is merely reserve resource for use in emergencies.

The cause of death then in suprarenal deficiency still remains an unsolved riddle. We are led back to the theories that prevailed before the potency of suprarenal extracts was discovered. Do these glands have a detoxicating function? Is the essential feature in death due to suprarenal deficiency a toxemia? If so, the toxin should be detectable, particularly since it is often potent enough to kill a dog within a few hours. Some early observations are on record which indicate that such toxin can be demonstrated. Abelous and Langlois[30] reported that the blood of guinea-pigs dying after suprarenal extirpation is fatal to frogs. In view of the possibility of the formation of various decomposition products, however, the burden of proof is on the experimenter to show that the toxin is specifically due to suprarenal failure. Negative results in such experiments are more significant than positive. The matter has recently been under investigation in our laboratory. The work is not entirely finished, but enough has been done to indicate that the blood of dogs that have just died of suprarenal deficiency is not toxic to frogs. Other observers have failed to detect a toxin by transfusion experiments.

We are finally thrown back to the vague conception of a failure of tissue metabolism as the most probable cause of death. The tissues that first exhibit weakness are the cardiac and muscular. The most satisfactory theory for the time being, therefore, would seem to be that the suprarenals contribute to the blood stream some unknown substance necessary to the metabolic processes of these active tissues. The best evidence indicates that this hypothetic substance is derived, not from the suprarenal medulla which supplies adrenin, but from the cortex of the gland. At any rate in animals in which the two parts of the gland are separate, death follows when the cortex homologue is removed, leaving the chromaffin tissue unharmed.[31]

[29] Battelli: Comp. rend. Soc. de biol., 1902, p. 1138. Gradinescu: Arch. f. d. ges. Physiol., 1913, 152, p. 203.
[30] Compt. rend. Soc. de biol., 1892, 44, p. 165.
[31] Biedl: Innere Sekretion, 1913, I Teil, s. 371.

One other line of evidence bears on the question as to the function of the cortex. In various sorts of sex-gland anomalies, hvpertrophy of this tissue is observed. Most striking, perhaps, is the fact that sexual precocity in children has been shown to be accompanied by marked suprarenal hypertrophy or hypernephromata.[32] In some experiments recently made,[33] evidence has been secured that feeding suprarenal substance to young animals leads to hypertrophy of the testes. Further experiments along this line may lead to significant results.

CONCLUSION

The fundamental question remains yet to be answered: Why does the removal of the suprarenal glands cause death? The trend of the evidence now available suggests that muscular metabolism is at fault. If that be true, the solution, like that of many other puzzling medical problems, rests with the biologic chemists.

[32] Glynn: Quart. Jour. Med., 1912, 5, p. 157.
[33] Hoskins, R. G., and Hoskins, A. D.: Arch. Int. Med., 1916, 17, p. 584.

SYNDROMES ASSOCIATED WITH DISTURBED HYPOPHYSIAL FUNCTION

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During the past 10 years an extensive literature has developed on the functions of the hypophysis. No attempt will be made to review this, but I shall try to confine my remarks to those clinical manifestations in which the hypophysis is supposed to play a rôle. Briefly stated. these clinical manifestations are acromegaly, the adiposogenital dystrophia, or Froehlich's syndrome, possibly Dercum's disease, the question of glycosuria, and diabetes insipidus.

In the work done on the hypophysis it has been clearly shown that this is an organ which is essential to life. Complete removal of the hpophysis is followed within from a few days to a few weeks by the death of the animal. Removal of the posterior lobe alone is not inconsistent with life. Some animals recover from the operation, go on, and show no special disturbance. The removal of the anterior lobe alone is followed by the same consequences as complete removal of the gland, that is, the animal lives for only a short time. If, instead of complete removal of the anterior lobe, a portion is removed, the animal recovers in an indefinite time, but shows certain developmental disturbances. If this operation has been performed on an adult dog, the animal becomes very fat, becomes rather stupid and dull, shows rather marked thinness of the hair, and sexual atrophy. If this operation is performed on a puppy, the animal shows disturbed skeletal development and, in addition, fatness, stupidity, thinness of the hair and failure of sexual development.

This experiment is of special interest as giving us a clue to the disturbance in the hypophysis which is probably responsible for the syndrome.

Turning to the clinical manifestations which are supposed to be due to the hypophysis, we shall take up first the question of acromegaly. Marie, in 1886, was the first to call attention to the possible rôle of the hypophysis in this condition, although previous to this time it had been well established that in giants the hypophysis was often unusually enlarged — out of proportion to the size of the person. In all prob-

ability, most of the giants of history were persons in whom the gigantism was, in a measure, due to the hypophysis. It is also known that after castration the hypophysis undergoes hyperplasia, and this is the explanation offered why eunuchs often reach unusual size.

In regard to this disturbance in the hypophysis being responsible for the condition of gigantism or acromegaly, without going into a discussion of both sides of the question, it is now generally considered that acromegaly, or gigantism, represents a hyperfunctioning of the anterior lobe of the hypophysis. In case this hyperfunctioning begins in adult life, we have simply over-development of certain bony structures, with very moderate increase in the soft tissues, that is, a clinical condition known as acromegaly. If, however, this disturbance of functioning in the hypophysis begins before maturity is reached, we have a general increased skeletal development, and the condition known as gigantism.

There is a possibility that certain forms of dwarfism are due to insufficiency of the hypophysis, inasmuch as necropsies on numbers of these persons have demonstrated tumors of the hypophysis. Efforts to produce these changes of growth in young animals by feeding them on extract of the hypophysis have been unsuccessful up to the present time.

Passing to the second condition, Froehlich's syndrome, we have in mind a disturbance of development characterized by adiposity, by thinness of the hair, by a thickness and blueness of the skin, rather dull mentality, sexual atrophy, in women, scant or absent menstruation, and in men, absence of sexual desire. If this disturbance arises early in life, before maturity is reached, we have, in addition, delayed or incomplete development of the bony skeleton.

Froehlich's syndrome may at times, in rare instances, be associated with acromegaly. According to Freudenthal, in about 1.5% of acromegalic persons there are disturbances present which also indicate Froehlich's syndrome. Sexual atrophy, which is a practically constant accompaniment of Froehlich's syndrome, is found in more than a third of the cases with acromegaly, showing that at least the sexual disturbances are common to both conditions.

In regard to the origin of Froehlich's syndrome, Froehlich himself ascribed this disturbance to a condition in the posterior lobe. Since that time practically all investigators have taken the same stand. Cushing has been a strong advocate of the belief that Froehlich's syn-

drome is associated with a disturbance of the posterior lobe, that is, a lessened functioning of the posterior lobe. He has expressed the belief that this adiposity is in some ways associated with an increased tolerance for sugar. According to his view, people with Froehlch's syndrome always show an increased sugar tolerance, and that sugar tolerance is a factor in the development of the fat.

While diabetes mellitus is very common, and is found in about 30% or more of the patients with acromegaly, it is never found with Froehlich's syndrome.

To study this question more closely, we turn to the postmortem findings of these patients with Froehlich's syndrome. Most of them have tumors in the hypophysis. These tumors are usually of a destructive character — carcinoma, sarcoma, cysts, and so on — that would indicate, if anything, a lessened functioning of that portion of the gland. However, on account of the peculiar location of the hypophysis in the sella, it becomes difficult in any particular instance to say whether a tumor has affected one or the other lobe. For instance, a tumor in the posterior lobe, by pressure, may disturb the function of the anterior lobe, so that the necropsy table has really furnished us little evidence regarding what particular part of the hypophysis is responsible for disturbances associated with new growths. The best evidence in regard to the location of this disturbance is that furnished by animal experiments; for instance, Cushing's evidence, where he removed a portion of the anterior lobe of the hypophysis, producing in dogs a condition practically identical with that we are accustomed to consider as Froehlich's syndrome.

Froehlich's syndrome must come from some disturbance of the anterior lobe. It is certain that the developmental disturbance known as acromegaly has its origin in the anterior lobe. It is probable that other such developmental disturbances have their seat in the anterior lobe.

The occasional association of Froehlich's syndrome and acromegaly have led Cushing and others to state that it would be highly improbable that the anterior lobe could give rise in the same person to acromegaly, which is a hyperfunctioning, and to Froehlich's syndrome, which is a hypofunctioning, but it seems to me it would not necessarily follow that Froehlich's syndrome is a hypofunctioning. It could possibly be a disturbed functioning of the cells of the anterior lobe. We know that these cells show great power to change. For instance, during preg-

nancy, certain cells in the anterior lobe undergo changes of a histologic character, sufficient to give them the name of the cells of pregnancy, and it is not improbable, as a result of this change, that the secretion of this cell may be disturbed. Time will show that in all probability Froehlich's syndrome does not originate in disturbances of the posterior lobe, but from a disturbance of the secretion of the anterior lobe.

The results of organotherapy in Froehlich's syndrome have never been striking. Cushing has reported some cases where apparently there was improvement in the patient's mental condition, but we know how difficult it is to draw conclusions in regard to mental condition, because the friends or parents of such persons are always optimistic. When any new method of treatment is tried, they are always ready to state that the patient is better than before treatment. Cushing has also reported some improvement in the sexual power of these persons, and some slight loss of weight.

Regarding operative measures in Froehlich's syndrome, they usually have been confined to removal of the tumors, or operations on tumors or growths to remove pressure. No special change has been noted in the developmental disturbances following these operations.

Regarding the 3rd condition, Dercum's disease, it is very doubtful whether this has anything to do with the hypophysis. Dercum's disease is also called adiposis dolorosa. It is true that in a large number of these patients who have come to necropsy, tumors of the hypophysis have been discovered, but disturbances in the thyroid are much more constant, and whether the thyroid or hypophysis has anything to do with Dercum's disease has yet to be determined.

Passing to the 4th condition, namely, the question of glycosuria, it has long been a question whether the hypophysis did not have something to do with sugar metabolism, for the reason that more than one-third of the patients with acromegaly show a glycosuria, and a larger percentage show a lessened sugar tolerance.

Cushing has advanced the theory that the sugar tolerance of these patients also rests in the posterior lobe of the hypophysis. I should say that the posterior lobe of the hypophysis is an important factor in sugar metabolism. When we have an increased function of the posterior lobe, the patient shows a lessened sugar tolerance, a lessened activity of the posterior lobe, an increased sugar tolerance.

Cushing has also expressed the view that this affect on sugar metabolism is due to a hormone. He bases this largely on the fact that

when he stimulates the hypophysis in the normal animal a glycosuria or a hyperglycemia occurs. When he sections the cord and then stimulates the hypophysis, the same glycosuria occurs afterward as before the cord was sectioned; that is, expressing the belief that it is not a nerve impulse, but something that travels through the blood, such as a ferment.

Cushing has also expressed the view that all patients who have Froehlich's syndrome probably show an increased sugar tolerance, and that Froehlich's syndrome is due to a lessened functioning of the posterior lobe.

These views of Cushing in regard to the relation of the hypophysis to glycosuria have not been generally confirmed, for instance, his position that the patients with Froehlich's syndrome all show an increased tolerance to sugar. Forschbach and Severin have recently studied the sugar tolerance in 2 patients with acromegaly: in one there was an increased sugar tolerance; in the other, a diminished sugar tolerance. They also studied 2 patients with Froehlich's syndrome, both with normal sugar tolerance, and 3 patients with tumor of the hypophysis, without developmental disturbances, and all of these showed increased sugar tolerance.

Bernstein has recently studied 2 cases with Froehlich's syndrome, both with normal sugar tolerance.

So that it has yet to be proved, or it would appear to be disproved, that Froehlich's syndrome is usually associated with an increased sugar tolerance.

We have recently had under observation a patient with diabetes insipidus and Froehlich's syndrome, in whom Woodyatt, with his new method of testing sugar tolerance, has found a normal sugar tolerance.

Regarding the effect of producing glycosuria in animals by the injection of the hypophysis, Cushing has maintained that the injection of the posterior lobe in animals is always followed by glycosuria. The earliest work on this subject was done by Bouchard, who obtained glycosuria in 80% of the animals. However, other workers have failed to produce glycosuria with either anterior or posterior lobe of the hypophysis. Lewis and I injected 30 rabbits, 15 with extract of the anterior lobe, and 15 with extract of the posterior lobe, and in only 1 of these were we able to obtain glycosuria. It might be stated too, that Keaton and Becht recently have shown that Cushing's theory in regard to hormones probably does not hold true. These observers have

repeated the experiments and have found that after cutting the splanchnics and stimulating the hypophysis a hyperglycemia did not appear, while the animals in which the splanchnics were not sectioned, but the hypophysis was stimulated, did show hyperglycemia, proving that, after all, it is probably a nerve impulse rather than a hormone that produces this condition. This question of glycosuria and its relation to the hypophysis is still in an unsettled state. We are not in a position to state what relation the hypophysis might bear in certain cases of glycosuria.

Concerning the last point to be considered, namely, the question of the relation of the hypophysis to diabetes insipidus, Magnus and Schaeffer called attention a few years ago to the diuretic effect of the posterior lobe of the hypophysis in certain animals. They injected cats intravenously and were able to obtain a diuresis in all instances. When they used dogs for this experiment, 7 out of 19, instead of having a diuresis, showed a marked lessening of the output of urine after the intravenous injection of the posterior lobe of the hypophysis, and in rabbits much the same thing occurred. In a certain number of the rabbits diuresis occurred, while in certain other rabbits a lessened output of urine followed. They found that giving it by mouth had no effect whatever in any of these animals, and when given subcutaneously, even in cats, which always reacted to intravenous injection, only 25% had a resulting diuresis. This is a rather severe commentary on the application of laboratory methods to clinical therapeutics, to know that directly after Schaeffer's publication appeared, extracts of the posterior lobe were placed on the market and recommended for use as diuretics, when taken by mouth.

For the last 2 or 3 years we have tried out pituitrin on a number of patients at the County Hospital, both normal and nephritic persons, to see whether we could get any diuretic action when administered intravenously. In not 1 person have we ever obtained any diuretic action. In the majority of patients we got a marked reduction of urine; in fact, they behaved exactly as the 7 of the 19 dogs of Schaeffer.

Recently, too, von den Veldt has given pituitrin subcutaneously to a number of persons, and has obtained exactly the same results, either no change in the output of urine, or else a marked reduction, and this reduction of the urinary output may reach as high as 50%.

I have gone into this somewhat in detail, because it has apparently a direct bearing on the question of diabetes insipidus. Diabetes insipidus,

or at least, a polyuria, can be produced in animals by many lesions. Taylor states that practically almost any lesion in the cerebellum, pons, or medulla is capable of exciting a polyuria in animals. Primarily, we find this condition associated more especially with processes at the base of the brain — tumors, or syphilitic basilar meningitis. That there is a relationship between certain cases of diabetes insipidus and the hypophysis would seem fairly certain.

Many patients with acromegaly show diabetes insipidus, and many patients with Froehlich's syndrome also show diabetes insipidus, and it is known that of the patients who show bitemporal hemianopsia, which is so frequently associated with hypophysial disturbances, 20 or 25% show diabetes insipidus. Recently, the interesting work of Simmons, at Hamburg, showed, in 1500 autopsies, that there were metastatic carcinomas in the hypophysis in 9, all in the posterior lobe, and in 3 of the 9 associated with diabetes insipidus.

Recently a woman has come under my observation who, a year ago, had a carcinoma of the breast removed, and who now has diabetes insipidus. She came to me stating that she wanted to know if she had diabetes insipidus. She was much interested in it, because a friend of hers a few years before had had a carcinoma of the breast removed, and died later of diabetes insipidus.

The work of Simmons, above referred to, is especially interesting because of these metastatic carcinomas being exceeding small — so small that they apparently could not exert any pressure on the anterior lobe — and we would suspect that a malignant growth in the posterior lobe of the hypophysis could do only one thing—if it affected the secretion, it must lessen that secretion.

Regarding the theory of diabetes insipidus, since Schaeffer's report on the diuretic action of the pars intermedia of the posterior lobe, all those people working with the hypophysis have assumed that in diabetes insipidus we are dealing with a hyperfunction of the pars intermedia, because Schaeffer was able to obtain a diuretic effect from its use. Since this work of Schaeffer's has been disproved, so far as man is concerned, and it has been shown that the posterior lobe of the hypophysis reduces the amount of urine rather than increases it, I think we must say that if the hypophysis is connected with diabetes insipidus, it is due to an insufficiency of the posterior lobe and not to a hyperfunction. During the past year or 2 there has been a great deal of support added to this view. At least 8 or 10 different reports have

appeared on the effect of administering pituitrin to patients with diabetes insipidus; that is, the administration of 1 c.c. twice daily will result in a reduction of the urine of 50% or more, which reduction will continue just as long as you give the patient the dose of pituitrin twice a day. We recently have had at the County Hospital a patient with diabetes insipidus and Froehlich's syndrome, who was passing 5 liters of urine a day. When given 1 c.c. of pituitrin subcutaneously twice a day, the urine was reduced 2500-2000 c.c.

This evidence points strongly toward diabetes insipidus being due to a lessened activity of the posterior lobe. In the patient above mentioned we determined the glyconitrogen in the blood during the period when passing large amounts of urine. It was large in amount, namely, 31 mg. It was again determined after 3 days' administration of pituitrin, and it had fallen to 21 mg.

If this observation should be confirmed, it would be interesting, as indicating that the increased output of urine is not necessarily associated with an increased output of nitrogen.

SUMMARY

Apparently acromegaly is due to a hyperfunctioning of the anterior lobe.

Froehlich's syndrome is due to some disturbance of secretion of the anterior lobe, the character of which has not been determined.

Whether the hypophysis plays any rôle in sugar metabolism or not has not yet been fully determined.

Apparently diabetes insipidus, when associated with the hypophysis, is due to an insufficiency of the posterior lobe.

DISCUSSION

DEAN D. LEWIS: This might well be called the era of ductless gland unrest, because men working with much the same material can interpret the findings in opposite ways. This is evidently due to several factors. One is that at the present time we have no index of the secretory activity of the ductless glands, and we have been apt to interpret hyperplasia as indication of excessive function. This is aptly illustrated in the case of the thyroid gland; Marine has obtained results from a study of dogs' thyroids, in which there is distinct hyperplasia, which he speaks of in terms of excessive secretion, but without adequate basis. Until we have some index by which we can bridge over the gap between hyperplasia, as indicated by cytologic study, and excessive secretion, we still shall have opposite interpretations of the same histologic appearances.

There are interesting points about the thyroid gland. First, we have to distinguish between two distinct types of perverted secretion; in one of these, the

primary hypersecretion, which was described by Kocher years ago, the enlargement of the thyroid, exophthalmic tremor, and tachycardia come almost simultaneously; the other might be called the type of exophthalmic goiter in which the symptoms develop in old but existing lesions in the thyroid, whether cystadenoma, carcinoma, or an inflammatory process. This type rarely has any exophthalmos associated with it. It is a type of disease, also, in which, so far as operative removal of the gland is concerned, we can expect a permanent recovery in 80% of the cases thus operated. That is altogether different from primary hyperplasia, in which it has been shown that after good operations we can expect only about 40% of cures. These statistics are based on 100 cases of consecutive hyperthyroidism with primary hyperplasia, the glands being removed by Judd in the Mayo clinic.

There are evidently two distinct types of thyroid lesions; one, primary and the other, secondary, differing as to symptoms and also as to the relation they bear to exophthalmos.

As far as regulation of the thyroid secretion is concerned, one would judge from the number of therapeutic measures which have been employed with apparent success in cases of hyperthyroidism that hyperthyroidism was easily controlled, because I do not know of any disease that has had more satisfactory results from almost any drug employed, from quinin hydrobromid to hydrastis canadensis.

The thyroid gland is variable on examination. One day it may be a vascular, purring gland; the next day, hard, no purring, and no pulsation in the vessels of the neck. In 24 hours it has passed from an active gland into a soft one. We must also recognize that hyperthyroidism tends to run a distinct course of exacerbations, extending over about 9 months, toward the end of which there is high activity followed by recrudescence. At the present time the only way we have to regulate the gland is by operative interference, either removal or ligation of the poles; the effect of the latter may depend on interruption of the nerve supply, because it does not seem probable that interruption of the vascular supply would have any great effect, for the vascular supply is so abundant that circulation ought to be practically reestablished by the time the ligature is tied.

There are interesting things about the hypophysis, and I believe it is the only ductless gland in which secretory activity is definitely related to cytologic changes in the cell. Miller has said that acromegaly is probably dependent on hyperplasia of the anterior lobe. I think he could have gone further and stated that acromegaly is due to hyperplasia of 1 type of cell in the anterior lobe. The reason that pathologists and clinicians have been so slow in recognizing the relation between anterior lobe hypertrophy and gross anomaly is because they have not paid enough attention to cell proliferation in the hypophysis, and there is much discussion still concerning the relation of cell hyperplasia to lesions in the hypophysis. If we study the hypophysis cytologically, we find in the anterior lobe two types of cells which stain distinctly, one, with acid dyes, which we call the acidophils, the other, the chromophils. It is striking that in relation to gross anomalies there is a distinct difference between these two types of cells, and also in relation to sugar metabolism. There have been but two cases of acromegaly reported in which anything but hyperplasia of the chromophil cells of the hypophysis or an adenoma composed of acidophil cells has ever been described, but no statement is made regarding the method of fixation or the time after death that the gland was examined. I think it has become generally

recognized that acromegaly is definitely associated with hyperplasia of the acidophil cells.

As to Froelich's syndrome, it is associated with a number of different tumors occurring about the hypophysis, in the interpeduncular space, or in the fossa.

Chromophobe cells are found normally in the infundibulum of the hypophysis. Stained with iron stains, they cannot be differentiated from mouth epithelium. These are the most frequent sort of interpeduncular cells. Some time ago I looked up the number of cases of interpeduncular cysts developing from these cells, associated with Froehlich's syndrome, and found 40% associated with Froehlich's syndrome, and 7% with diabetes insipidus.

It is not a far cry for Cushing to say that in the posterior lobe of the hypophysis there is a substance which acts much as suprarenal secretion, and probably has the same result on sugar metabolism, but it is interesting that practically the only tumor associated with the decreased sugar tolerance is a chromophil adenoma occurring in acromegaly. If a tumor develops in the anterior lobe, it must at some time make pressure on this pars intermedia, and sometimes must destroy it, so it would pass readily from increased to decreased sugar tolerance of acromegaly, which practically never occurs. The chromophobe adenoma and interpeduncular cysts in the anterior lobe must also at some time make pressure on that, and one would expect, early in the course, a decreased sugar tolerance, and later increase, but practically it does not work that way.

It seems to me we have in the hypophysis the most striking relation of any ductless gland in the body between distinct cytologic changes and anomaly in overgrowth.

As far as diabetes insipidus is concerned, as Miller has said, that is still an unsettled question. I have had opportuuities to examine serially the 3rd ventricle from 18 dogs in which operations had been done, with an attempt to produce diabetes insipidus. Not one of the dogs in which a total destruction of the pars intermedia had been made developed diabetes insipidus. The dogs that did have diabetes insipidus were dogs in which distinct remnants of the pars intermedia were always found in the flood of the 3d ventricle. The easiest way to produce diabetes insipidus in dogs is merely to expose the hypophysis through the pharynx, and heat the surrounding structures with a cautery—burn the anterior lobe, if you wish—without any attempt at destruction. In the pars intermedia we have no indication of secondary activity, but we know that the pressor substance appears in the pars intermedia about the 5th month in the pig, and there is some clue to connect function with cytologic changes.

I should doubt the ability of any one to differentiate the small glands in the posterior lobe from carcinoma.

A. J. CARLSON: I agree with Hoskins' conclusion as to the untenability of the tonus theory of the suprarenals, a theory based on erroneous physiologic data. I wonder, however, about the nature of the pressor substance, recently described by Whipple in the cortex.

I am not familiar with the clinical manifestations of hypophysis disease, but I would challenge Miller's statement that the hypophysis is necessary for life, in the sense that the parathyroids are necessary for life, or the suprarenals are necessary for life. I thought so a few years ago. I think most of us were similarly impressed by Cushing's experiments. I thought that question settled.

A few months after Cushing's demonstration of his dogs I went to Vienna, and there Aschner showed his dogs that were completely hypophysectomized one or two years before and were still living. Since then he has published a monograph on the subject. Cushing says Aschner did not completely remove the gland, and Aschner says that Cushing's dogs that died were killed by trauma of operation. But, after all, that is not the important question, and there is no doubt that the hypophysis is a physiologically important organ, and that was the point that was dwelt on.

THE OXIDATION OF CARBOHYDRATES

JULIUS STIEGLITZ
March 10, 1916

The purpose of this paper is to give an introductory statement on a part of the theory of the chemistry of carbohydrates that might serve to illuminate some of the important physiologic and medical phases of the subject, which are to be presented by Drs. Woodyatt and McGuigan. Quite innocent of any exact medical knowledge of the subject, I hope that the merely chemical prelude may prove helpful.

The rôle of carbohydrates in our food is to furnish energy for work and heat for warmth, and they accomplish this purpose essentially by the oxidation of the glucose which carbohydrates yield. Anything that interferes with this combustion of glucose is bound to lead to some form of the condition which is called diabetic. For this reason I wish to make the central feature of my discussion a development and explanation of some of the fundamental conditions controlling the oxidation of glucose outside of the body. The point of view thus obtained should be at least suggestive to the actual investigators of the pathologic condition.

It may be of interest to have this theory of the oxidation of glucose presented from what we may call the modern or electric point of view. In order to do this, I shall first develop in outline two or three fundamental principles of chemical theory which have been established in comparatively recent years and which are necessary for the discussion of the main topic.

In the first place, to get at the heart of the question of the oxidation of glucose, we must ask the question: What is the essential nature of oxidation? An extensive category of descriptive facts has been enumerated in the definition of this fundamental process, as, for instance: "oxidation consists in the absorption of oxygen, or of similar elements such as chlorin, bromin, sulphur, nitrogen, etc., or in the loss of hydrogen or its equivalent." Chemistry and physics have penetrated deeper than this merely descriptive definition into the essence of oxidation. All of the facts enumerated in the old definition are from the present point of view sequelae, rather than the process itself. Oxidation, and its complement reduction, are intra-atomic phenomena and

root in the very structure of the atoms. As a result of the discovery of the unexpected properties of radium, other epoch-making discoveries by Thomson, Rutherford, Ramsay, and others have led in a few years to the positive conclusion that all matter is essentially electric in character. Each atom consists of nicely balanced positive and negative units of electricity and these units of electricity are the common components of all elements. They are indeed the only really elemental forms of matter and the so-called elements differ from one another only by the number of these electric units contained in the atoms. Thus, the hydrogen atom is considered to consist only of a single positive unit and a single negative unit or electron, which probably oscillates around the positive core. The oxygen atom, in turn, seems to contain 16 positive units and the same number of electrons. The electron or negative unit is extremely minute, about $\frac{1}{1800}$ the mass of the hydrogen atom, the positive corpuscle much more massive in comparison, having about the weight of the hydrogen atom. The minuteness of the negative electrons gives them free passage where more massive particles are hindered in motion, and an electric current through a wire is essentially a current of electrons moving through the wire with a high speed.

Each atom then is a kind of constellation of positive corpuscles and negative electrons, a conception which brings us directly to the modern definition of oxidation. I had better develop this definition in connection with a simpler oxidation, the combustion of hydrogen and oxygen to form water, before taking up the oxidation of glucose. Systems like the hydrogen atom and the oxygen atom need not be absolutely stable; they may become more stable, either by the escape of one or more of these extraordinarily mobile electrons from the atom or by the capture and absorption of one or more electrons from neighboring atoms. This possibility indeed represents the true relations exactly. For instance, the hydrogen atom has a proved, very great tendency to become more stable by ejecting an electron, leaving a positively charged ion H^+, whereas the oxygen atom has even a greater tendency to absorb two further electrons, becoming negatively charged $^-O^-$. Whenever hydrogen atoms discharge electrons and become positive

$$H \rightarrow H^+ + (e)$$

hydrogen is oxidized. Whenever any atom whatsoever loses electrons, it is oxidized — that is the modern definition and conception of oxidation. On the other hand, whenever an atom absorbs electrons, it is reduced — the reverse of oxidation. Thus, oxygen, by absorbing two

electrons per atom, is reduced. Incidentally, but only as a sequel, the charges produced by forming H^+ and $^-O^-$ enable these charged particles to combine with each other to form water, $H^+—^-O^-—^+H$; the atoms are held in the molecule by electric attractions, with a force that Helmholtz calculated to be 70,000 billion times as great as the force of gravity under the same assumed conditions. The essential thing in the oxidation of hydrogen by oxygen is the loss of electrons by the hydrogen and their absorption by the oxygen — the actual union of H^+ and $^-O^-$ is merely incidental and a sequel, and not even a necessary sequel, as is shown by the fact that there is free H^+ in solutions of the acids, and free $^-O^-$ ^+H, and no doubt also some free $^-O^-$ in solutions of the bases.

If this development is correct, we must anticipate that a current of electricity can be produced by means of a device which would enable the electrons lost by hydrogen to migrate to oxygen through a wire. There is nothing easier than to accomplish this. The hydrogen that does not escape into the air in this experiment is being oxidized by satisfying its tendency to give off an electron from each atom. It gives these electrons off to the platinum gauze through which the gas is passing, and the electrons escape through the connecting wires and this voltmeter to the other gas electrode, where they are absorbed by the oxygen atoms of the air, reducing the oxygen to $^-O^-$. This flow of electrons is the current observed, and the voltmeter is an instrument to measure the intensity of the action. We thus have combustion of hydrogen and oxygen by what is called 'cold' or 'electrolytic combustion.' It leads to the formation of water, just as in flame combustion, but by this device, keeping the elements apart, we have been enabled to analyze the process and recognize its really essential elements. It is characteristic of this method of electrolytic combustion, in the first place, that it takes place readily at ordinary temperatures under the conditions employed. In the second place, this device, with the produced electric current passing through the voltmeter, represents a machine — the current lifts and moves this needle, and on this rough model a perfect machine could be constructed which would give, as Nernst has calculated, almost the theoretical yield, 100%, of the power in the hydrogen and oxygen consumed. If the combustion of hydrogen by the flame or the explosion method were utilized to run a machine, such a machine would yield at best, perhaps only 20-30% of the power in the oxygen and hydrogen, exactly as the best gasoline engines give, at most, 30% of the power in the gas consumed, and waste 70%. These

facts of maximal yield of energy in cold combustion are characteristic of electrical combustion as against ordinary flame combustion. It is evident, too, that if the transfer of electrons did no work, we should get, as usual, its equivalent in heat. This would be the case if we allowed hydrogen and oxygen to combine under the ordinary conditions.

The combustion of carbohydrates in our bodies shows both of these fundamental characteristics: cold combustion — for we cannot use the high temperatures of a flame in our bodies — and an almost perfect yield of the total amount of energy found in the consumed carbohydrates. To this extent and in these fundamental respects, our body processes resemble this contrivance much more than they do the furnaces with which of old and perhaps even in some lecture rooms of this day our bodies are compared, with regard to the consumption of food.

Having developed the fundamental conception of oxidation that modern chemistry deals with, as an intra-atomic loss of electrons, I wish to explain one further fundamental conception — chemical equilibrium — and then I shall apply the two conceptions to the oxidation of glucose.

The oxidation of hydrogen, $H \rightarrow H^{+} + (\epsilon)$, is a reversible process: We can generate hydrogen from water by forcing a strong electric current through it. In the apparatus as it stands, some of the hydrogen, in contact with the platinum gauze is giving up an electron per atom, being oxidized to H^{+}, and the electrons charge the gauze negatively and flow off through the wire connections. If we connect this same gauze with the negative pole of a lighting circuit we charge the electrode where we were consuming hydrogen much more strongly negatively by crowding electrons on to it, and under these conditions our action is completely reversed. We are now getting hydrogen gas from this same electrode, and current is consumed. The conditions, qualitatively, are the same as before — in the solution H^{+}, on the gauze negative electricity or electrons — we have simply changed the concentration or mass of the electrons on the gauze: By making it excessively great we have crowded back the reaction $H \leftarrow H^{+} + (\epsilon)$. One may aptly compare this change with the picture of three or four men of a football team pushing a single man down the field: add five or six teammates to the single man, and the march will go in the opposite direction. In between these two extremes, however, there should be a point where

the two opposing forces should be exactly balanced. Applying this to our system we have:

$$(1)\quad H \rightarrow H^{+} + (\epsilon)$$
$$(2)\quad H \leftarrow H^{+} + (\epsilon)$$

and there must be a point of equilibrium, where the masses are such that the reversed actions $H \rightleftarrows H^{+} + (\epsilon)$ go exactly at the same rate and thus result in a condition of no change or equilibrium. From that point we may force the action in either direction by changing merely the masses or concentrations of the components. We have already shown that a great increase in the mass of electrons on the gauze will drive the reaction back. Similarly, an increase in the mass of H^{+} around the gauze should at least reduce the intensity of the action by which hydrogen loses electrons, forms H^{+} and produces a current. This is easily accomplished by adding any strong acid, like sulphuric acid, to the liquid around this electrode experiment.

One other illustration, to clinch our conception of equilibrium and the disturbing of equilibrium: Carbon dioxid is somewhat soluble in water and combines with it to a certain extent, and, vice versa, we can recover the carbon dioxid from the solution, that is, reverse the action, for instance, by simply passing a current of air through the solution. We have:

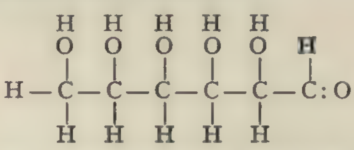
$$CO_2 + H_2O \rightleftarrows H_2CO_3$$

If we increase the concentration (pressure) of the CO_2 we get much more H_2CO_3, as in soda water, beer, or champagne. Or, if we add alkali and convert the H_2CO_3 into sodium carbonate and thus interfere with the reversed reaction, we also can get a much greater amount of CO_2 into solution, in the form of sodium carbonate.

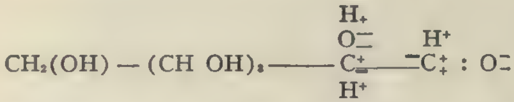
Considering, at length, the oxidation of glucose from the point of view of these ideas, if oxidation is an electric phenomenon inherent in definite changes of specific atoms, we must find that the oxidation of glucose must, like the oxidation of hydrogen, be a source from which we can derive an electric current, and that the intensity of the current, moreover, must be subject to equilibrium conditions of the same character as we have just now taken into account. All of these expectations are fulfilled and, moreover, the voltmeter is a device to determine and demonstrate sharply the optimum conditions for the oxidation. Glucose, dissolved in a neutral salt solution (sodium chlorid) into which a platinum electrode is allowed to dip, and placed against an electrode through which air is bubbling, gives a scarcely perceptible current or potential (experiment). If we add a small amount of alkali to the oxy-

gen electrode, its effect, if any, is to depress somewhat the potiential (experiment), for the same reason that acid drove back the tendency of hydrogen to be oxidized. If now we add the same small amount of alkali to the glucose solution, we find a remarkable increase in the potential results (experiment). It is obvious, first, that we can get a current from the oxidation of glucose, as was anticipated, and further, that alkali increases most decidedly the sensitiveness of the sugar to oxidation. It decreases the oxidizing power of the oxygen, but the gain for the sugar is so great that this gain much more than offsets this slight loss. The result is the more impressive because this needle registers exponents, not numbers only. Thus, if the oxidation of glucose in neutral solution were measured, for instance, by the number 10^1, its oxidation now, in alkaline solution would be represented by the number 10^x, that is to say, the glucose is 10^x times as sensitive as it was before.

It is evident that alkali must have some specific effect on glucose. In a glucose solution we have as an active component, a molecule of the following composition and structure:

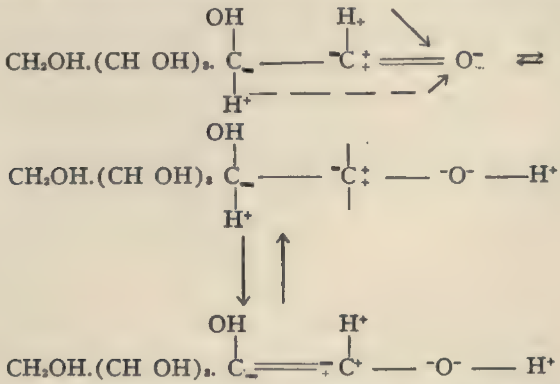


According to the electric conception of matter, the atoms are held in the molecule by electric forces, and we have, limiting ourselves to the two most significant groups, the real sugar group, and to the significant charges:



This form is evidently not very oxidizable, perhaps even not oxidizable at all. The only atoms, in fact, that could be oxidized are the carbon atoms — oxygen in the form $^-O^-$ is perfectly stable; all the hydrogen H^+ is already fully oxidized. Further, those carbon valences that are positive are also already oxidized, as they have lost electrons at those points to form positive charges. For this group — if we do not tear the carbon atoms apart, a consideration to which we will return — the only oxidizable components are the negative parts of the carbon atoms (indicated by heavy type). These negative charges are, however, not

exposed; they are masked by the hydrogen H^+ held by them, just as effectively as we mask iron in ferrocyanids, or in certain iron protein preparations. Now, the heavy negative charge on the oxygen of the $C^{+}_{+} :O^{=}$ group must have a certain pull on the positive hydrogen H^+ in its immediate neighborhood. That must lead to a condition of equilibrium, with which chemists are quite familiar, and the components of which have been actually isolated and studied in simpler cases:



In the two new forms we have the negative charges (indicated by heavy type) of both carbon atoms exposed to oxidation, to the loss of the electrons: in the first form by virtue of a Nef bivalent carbon atom, in the second form by a sensitive ethylene or double bond grouping. It is quite probable that the faint oxidation of glucose in neutral solution is primarily due to the presence of the traces of these forms in equilibrium with the inert aldehyd. When we add alkali, it yields salts of these active forms and thereby shifts the equilibrium to these forms, just as alkali moved the carbon dioxid and water equilibrium over so as to form sodium carbonate in quantity. These salts are, of course, just as oxidizable as are the hydrogen derivatives (or possibly more so), and the tremendous increase in mass of the oxidizable component corresponds to the increase in potential.

It does not require much alkali to have this effect: the alkalinity of the blood and the influence of enzymes — which often have the effect of powerful alkalis — probably suffice to account for the ease of oxidation of glucose in a healthy body.

If we let this system stand for some time, we notice an extremely interesting change. Whereas ordinary electric batteries unfortunately tend, by use, to run down, this one shows, by contrast in the course of

time a decided increase in power — an increase, which is more impressive because the voltmeter registers exponents and not merely numbers. This increase can denote only one thing, namely, that in the course of time, by a slow process, some more oxidizable substance or substances than glucose itself are formed from it — either by the action of the alkali alone on the glucose, or by the combined action of alkali and oxidation. Alkali alone is known to break up glucose into smaller fragments — by virtue of equilibrium disturbances, much the same nature as the simplest ones discussed before; alkali with oxidation must cause the decomposition to proceed still more easily. Whichever is the course of the reaction by which the smaller, more sensitive fragments are formed — and theoretically, both courses outlined must be followed simultaneously — we still find by the voltmeter that the alkali is the vital element in sensitizing glucose for oxidation by oxygen by a series of disturbances of the equilibrium in which glucose is ordinarily stable.

The device, with a small amount of alkali added to the glucose, is roughly diagrammatic, for instance, of a healthy active muscle or blood stream — wherever the oxidation of glucose may be found to occur. If we add an acid like lactic acid or carbonic acid to the alkaline sugar solution (exp.) it is interesting to note the fall of potential: this is characteristic of our tired muscles, of the condition, possibly of a diabetic patient. It has long been known that lactic acid interferes with the oxidation of glucose, but this is the only positive demonstration, by analysis, that its effect is due to its effect on glucose and not on the oxidizing components of the muscle or blood.

Before leaving the subject of the oxidation of glucose itself, I may add that Professor A. P. Mathews and Dr. Bunzel found that the oxidation of glucose by as powerful an agent as bromin is also favored in strongly acid solution. The conditions in the body are probably never strongly acidic, but the results of their work agree altogether with the theory of the oxidation just given in simpler cases, since strong acids, as well as alkalies, have been found to disturb equilibrium conditions in favor of the formation of the sensitive enol-forms which are oxidized easily. But the results of the work of Professor Mathews and Dr. Bunzel confirm the conclusion that the alkaline oxidation is always the most powerful.

If we substitute levulose (fruit-sugar) for glucose we make exactly the same kind of observations as with glucose — the intensity of the

oxidation in alkaline solution is in one experiment only slightly less than for glucose under the same conditions. This would indicate that the main component being oxidized at the outset is rather the ethylene derivative, which fructose also can form, than the Nef bivalent carbon derivative, which fructose can form only after being changed into glucose. On the other hand, cane-sugar, which, intact, has no sugar group and is simply a polyvalent alcohol and acetal, gives even in alkaline solution only a comparatively small potential (exp.), a potential which is due to the sensitizing of the alcohol groups, but which lacks the strong reducing power of the sugar group, which has been demonstrated for glucose and fructose. This shows plainly that the point of attack by the alkali and the oxidizing agent is indeed the sugar group, a conclusion which is confirmed by other observations.

There is no doubt that a sugar like l-glucose or gulose, which as such is not oxidizable in the body, but must first be transformed into d-glucose, would give directly, when tested by this instrument, the same order of oxidizing potential as glucose itself, in the same way as does arabinose, a pentose, also nonusable in the body (exp.). This shows that in the body there must be at least one further important factor determining the oxidation of carbohydrates, a factor which is almost certain to be found in the enzymes that control oxidation in the body, and which act specifically on definite sugars, perhaps on account of the stereochemic relations between the enzymes and the sugars they act on.

CONCLUSIONS

1. The oxidation of glucose is an intra-atomic electric phenomenon involving the loss of electrons by the carbon atoms of glucose and is essentially of the same character as is the oxidation of a simple element like hydrogen or zinc. The production of an electric current was anticipated from this point of view and realized.

2. The oxidation of glucose is enormously accelerated by the presence of alkali and it is retarded by the presence of neutralizing acids. The alkali acts by shifting the equilibrium conditions of glucose so as to give a much larger concentration of the oxidizable component, by exposing the negative charges of the carbon atoms involved.

3. The important increase in potential in the course of time shows that the decomposition products resulting from the action of alkali

and oxidation on glucose, or of alkali alone, are much more oxidizable even than glucose itself.

4. The fact that such sugars as are not directly oxidizable in the body give the same order of high potentials, when investigated in this way, shows that there is some fundamental specific factor, probably the oxidizing enzymes, whose influence in the body is of paramount importance in the physiology of the oxidation of carbohydrates.

SUGAR METABOLISM

Hugh McGuigan
March 10, 1916

The history of carbohydrate metabolism is so closely related to the study of diabetes that the two cannot well be separated. This close relationship was not realized, however, until Dobson[1] in 1774 demonstrated the presence of glucose in the urine of diabetics. About the same time Lavoisier[2] proved that oxidation of foodstuffs is the same within the body as outside of it, and that animal heat is derived from the oxidation of the body's substance. These discoveries mark the beginning of the modern era of carbohydrate metabolism. The term 'metabolism' was introduced by Liebig[3] in 1842, and includes the total chemical changes of foodstuffs under the influence of the enzymes and living cells of the body.

Diabetes has been known from the earliest times. Aretaeus[4] in the 1st century named it and left a classic record of the symptoms. Susruta[5] about the 7th century know of the peculiar odor and sweet taste of diabetic urine. But Paracelsus[6] (1493-1541), the founder of chemical pharmacology and therapeutics was apparently the first to attempt a closer investigation of it. He evaporated a liter of diabetic urine and found that it contained 4 oz. of what he called salt (more than 4 times the normal amount). The work of Paracelsus also marks the beginning of the application of chemistry to the study of medical problems. From his discovery, Paracelsus taught that the blood of diabetics contained a salt which, when eliminated by the kidneys, caused polyuria. In consequence of the salt in the blood being the real cause of the disease, he taught that the treatment need not be directed against the kidney, but at a cause farther back. The kidney, however, had been considered the cause of diabetes since the time of Galen,[7] and the advice of Paracelsus fell on deaf ears.

[1] Medical Observations and Inquiries by a Society of Physicians in London, 1776, 5, pp. 298-316.
[2] Rubner: Ztschr. f. Biologie, 1893, 30, pp. 73-142.
[3] Die Organische Chemie in Ihrer Anwendung auf Physiologie und Pathologie, 1842, p. 9.
[4] Bernard: Le diabète et la glycogenese animal, 1877, pp. 57, 145.
[5] Lusk: Science of Nutrition, 1909, p. 271.
[6] Lepine: Le diabète, Alcan, 1909, p. 2, 2. Garrison: History of Medicine, 1914, p. 139.
[7] Quoted by Lepine: Le diabète, p. 1. Also Bernard, loc. cit., p. 145. Original reference quoted by Bernard-Galen, Lib. xxvi De locis mal affects, Cap III.

Willis[8] in 1674 emphasized more strongly than his predecessors the sweet taste of diabetic urine, and Dobson a century later (1774), like Paracelsus, evaporated diabetic urine and concluded that the residue was analogous to sugar. Dobson is generally credited with the discovery that diabetic urine contains sugar, but not without protestations and accusations of plagiarism. There is no doubt that about the same time others reached the same conclusion. In 1815, the chemist, Chevreul,[9] demonstrated the identity of grape sugar and diabetic sugar. Dobson also noted that the serum of diabetics had a sweet taste, and Bernard,[10] 70 years later (1847), proved that the blood of diabetics contained sugar.

The rôle of Bernard in the field of sugar metabolism is especially interesting. While he was an intern in the Paris hospitals under Magendie,[11] the therapy of Broussais[12] and Rasori[13] was still in vogue, and although Magendie taught against it, bleeding for almost every disease was a routine treatment. Liters of blood drawn for the therapeutic effect were available to any investigator.[14] It is therefore quite reasonable that Bernard's thesis for the doctorate should be an investigation of the blood sugar. Although also credited with the discovery of sugar in the normal blood, in his thesis he contended that normal blood did not contain a trace of sugar.[15] It was only after a controversy with the chemist Figuier that he finally proved sugar to be a constituent of normal blood, and that blood without sugar is decidedly abnormal.

His failure at first to detect sugar, when satisfactorily explained, led directly to another important discovery, the phenomenon of glycolysis. In his first work he used blood that had stood in the hospital wards 12-24 hours.[16] When he worked with freshly drawn blood and found that it contained sugar, he was quick to infer that the sugar in the old blood had disappeared on standing. Investigation easily proved the truth of his conjecture. This phenomenon, interesting in view of the later work of Cohnheim and others, on the mechanism of sugar oxidation in the body, was the foundation of still further research by Bernard.

[8] Bernard: Le diabète et la glycogenese animal, 1877, pp. 58, 145.
[9] Annales de Chemie, et de Physique, 1815, 95, p. 319.
[10] Le diabète et la glycogenese animal, 1877, p. 127.
[11] Bernard: Le diabète et la glycogenese animal, 1877, p. 226.
[12] and [13] Garrison: History of Medicine, 1914, p. 139.
[14] Bernard: Le diabète et la glycogenese animal, 1877, p. 221.
[15] Quoted from Lepine: Le diabete, pp. 12, 13.
[16] Bernard: Le diabète et la glycogenese animal, 1877, p. 207.

Before this time (1821) Tiedemann and Gmelin[17] discovered that during the digestion of starches in the body, glucose was formed, and they deemed sugar a normal ingredient of the blood (1826); an observation confirmed by Magendie and by Frerichs[18] in the early 40's, several years before Bernard began to work. The origin of blood sugar, known to be identical with glucose, was therefore apparent.

The presence of sugar in normal blood being established, there remained to be determined, 1st, the changes, if any, which the sugar undergoes during its passage through the intestinal wall; 2nd, its condition in the blood and the changes through which it passes before oxidation in the body; and, 3rd, the differences between the normal and the diabetic so far as blood sugar is concerned. It is not always convenient to follow the researches on these phases of the subject in chronological order.

The most important and fundamental work in sugar metabolism was the discovery of glycogen by Bernard[19] (1857). After many attempts to produce diabetes artificially, he found that puncture or injury of the 4th ventricle causes glycosuria.[20] He then attempted to find the source of the sugar which appeared in the urine, and soon discovered that arterial blood contains more sugar than venous blood. When the carotid artery contained 0.12%, the jugular vein contained 0.08%. The relation of the femoral vein and artery were similar. It was evident, therefore, that sugar was lost from the blood to the tissues during the circulation.

With a flexible rubber catheter or sound, he was able to make soundings and to take blood for analysis from almost any point of the venous circuit.[21] He introduced the sound into the jugular vein and pushed it down into the right heart and found that the venous blood in this region contained as much sugar as the arterial blood. It was clear that somewhere between the femoral vein and the right heart, sugar was added to the blood. To definitely locate the source of this addition he passed the sound through the heart and down to the level of the kidneys and found that the venous blood at that point contained 0.08% sugar. The sound was then carefully withdrawn to the level of the hepatic vein, where the blood was found to contain 0.14% sugar.

[17] Die Verdauung nach Versuchen, 1826, 1, p. 184.
[18] Bernard: Le diabète et la glycogenese animal, 1877, p. 159.
[19] Le diabète et la glycogenese animal, 1877, p. 162, ff. Compt. rend. Acad. d. sc., 1857, 44, p. 578.
[20] Bernard: Lecons de physiologie experm. appliquée a la medicine, 1855, Vol. I, p. 288. Lecons sur le sytème nerveux, 1858, 1, p. 397; 2, p. 528.
[21] Bernard: Le diabète et la glycogenese animal, 1877, pp. 281, 288. Lepine: Le diabète, 25, p. 25.

In another experiment, he introduced the sound into the crural vein to the level of the hepatic vein and with a syringe aspirated the blood for analysis. It contained 0.266%, while the inferior vena cava contained 0.088%. By these and other experiments he proved that the liver was the source of the added sugar.

He also found that if the fresh liver were quickly removed from an animal and thrown into boiling water, only small amounts of sugar were obtained. But there went into solution in the water a substance which made an opalescent solution and which when boiled with acid, or acted on by saliva, yielded a reducing sugar. Bernard was able to isolate and study this substance which he called glycogen. The increased discharge of this substance from the liver is believed to be the commonest cause of most forms of hyperglycemia, at least of those that are transitory.[22] Bernard thought that the increased blood flow through the liver was chiefly responsible for the hyperglycemia by bringing about an increased glycogenolysis.[23] Others have thought it due to changes in glycogenesis.

Since the condition of the glycogen in the liver seems to be immediately responsible for the hyperglycemia, it is important to know whether the increased glycogenolysis or decreased glycogenesis is due directly to the liver itself or whether it is due to defections in other organs that act indirectly on the liver. Most other organs have been incriminated in the trouble.

Nicolas and Gueudville following Rollo[24] regarded diabetes as a deviation of the digestive functions with the initial lesion in the intestine, and perhaps due to changes in the gastric juice. Although they founded a system of treatment based on this theory, they never attempted to support it by experimental evidence. Croftan[25] thought that he obtained evidence showing that the intestine is necessary for the polymerization of sugar and the formation of glycogen. According to his theory, the sugar must pass through the intestinal wall, otherwise no glycogen can be formed from it; inferentially, the intestine may be the seat of the metabolic disturbance. Pflüger[26] denies Croftan's contention absolutely, and Macleod[27] rejects his evidence as entirely inadequate.

[22] Macleod: Diabetes, Its Pathological Physiology, 1913, p. 55.
[23] Bernard: Le diabète et la glycogenese animal, 1877, p. 457. Ibid., Lecons sur le système nerveux, 1, p. 477.
[24] Bernard: Le diabètes et la glycogenese animal, 1877, pp. 60 and 76.
[25] Arch. f. d. ges. Physiol., 1909, Vol. 26, p. 416.
[26] Arch. f. d. ges. Physiol., 1909, Vol. 26, p. 416.
[27] Macleod: Diabetes, Its Pathological Physiology, 1913, p. 121.
[28] Arch. f. d. ges. Physiol., 1907, 128, p. 1.

There is also much circumstantial evidence against the intestine's importance in the glycogen formation. Grube[28] showed that the liver polymerizes only the monosaccharids. Again, if any of the polymerized forms of sugars, dextrins or starch be injected into the blood, the diastases of the blood immediately break them down into the simple sugars. What is not hydrolyzed is excreted by the urine or intestine. It would seem, therefore, that if any polymerization of the sugar from the intestinal tract takes place while passing through the gut wall, it would be again hydrolyzed in the blood and energy lost in such a mechanism. However, it is still possible that some other modification of the sugar takes place to aid in glycogen formation.

Against such assumption, however, is the condition of sugar in the blood. The weight of evidence favors the opinion that sugar in the blood exists in the same state as it exists in a water solution. The proof of this is as follows: Rona and Michaelis[29] have shown that the proteins of the blood can be precipitated by colloidal ferric hydroxid, and when this is done all of the sugar is in the filtrate. By this method, the minimal amount of change in the proteins occurs and suggests strongly that blood sugar is uncombined. Many others have dialyzed the freshly drawn blood and have been able to dialyze out all of the sugar. If this were a colloidal form, such a separation would be improbable. Even such mild manipulations, however, may break up weak combinations of the sugar and the proteins, and so to get still nearer the actual condition, von Hess and myself[30] dialyzed the normal circulating blood and found that all of the sugar can be dialyzed out. The apparatus which we used was a modification of the dialyzing apparatus used by Abel and his co-workers,[31] and consists essentially in placing a segment of an artificial artery, composed of collodion, between the cut ends of a normal artery in such a way that it can be immersed in water or saline and dialysis accomplished while the blood is circulating within the animal. The general technic and the illustration of the instrument will suffice here.[32]

The general technic of the experiments was as follows:

A dog of moderate size was anesthetized; appropriate 3-way cannulas were tied in the carotid artery and external jugular vein on the same side or in the femoral vessels, and the dialyzing apparatus was then attached by rubber tubing, the glass tubes being approximated end to end. A saline flushing bottle was connected to the 3rd way of the arterial cannula and a short exit tube, with

[29] Biochem. Ztschr., 1908, 7, p. 329; 1909, 16, p. 60.
[30] Von Hess and McGuigan: Jour. Pharmacol. and Exper. Therap., 1914, 6, p. 45.
[31] Jour. Pharmacol. and Exper. Therap., 1914, 5, p. 275.
[32] Details are given in Jour. Pharmacol. and Exper. Therap., 1914, 6, p. 45.

a pinch clamp, fastened similarly to the venous cannula. The dialyzing tubes were then emptied of air by filling with normal salt solution. Likewise the enclosing jacket was filled with saline sufficient to immerse the dialyzing tubes. By removing the clamps from first the vein, then the artery, blood circulated through the tubes and dialysis commenced. The intra-jacket air pressure was raised sufficiently to cause a pulsation in the colloidal tubes synchronous with that of the carotid. This is a very important factor in preventing coagulation, for clotting often resulted when a good pulsation was not obtained. From time to time, or continuously, the dialysate was mixed by means of the movable bulb attached as illustrated in accompanying figure. Continuous mixture of the dialysate shortened enormously the time necessary for sugar equilibrium. In actual experiments clotting in the apparatus was a negligible factor although occasionally, when the blood current was slow, the vessels were clamped temporarily, and the dialyzing system flushed with saline. Because the blood pressure in such a dialyzing system is high, leaking of the blood at the junction of the collodion and the glass tubes was the principal source of trouble in the early trials and in such instances necessitated the relegation of the leaking joints and resealing with collodion.

The time required for a sugar equilibrium between the blood and the dialysate varied greatly according to the number of mixtures made in the dialysate. A sugar equilibrium could be obtained only after 10 hours when the dialysate was not mixed, in not less than 3½ hours when the dialysate was mixed every 2 or 3 minutes, but in less than 1 hour's time if the dialysate was mixed continuously (about every 8 seconds). The sugar equilibrium was determined by noting when no change in the ratio of the plasma sugar to the dialysate sugar occurred.

At the end of dialysis, about 100 gm. of blood were drawn into a flask containing 0.3 gm. of powdered potassium fluorid, shaken, centrifuged for 5 minutes at 3000 revolutions per minute, and the plasma pipetted off. The proteins of the dialysate and the various blood samples were precipitated, immediately after each was obtained, with acetic acid and sodium sulphate, the object being to prevent any glycolysis of the blood sugar.

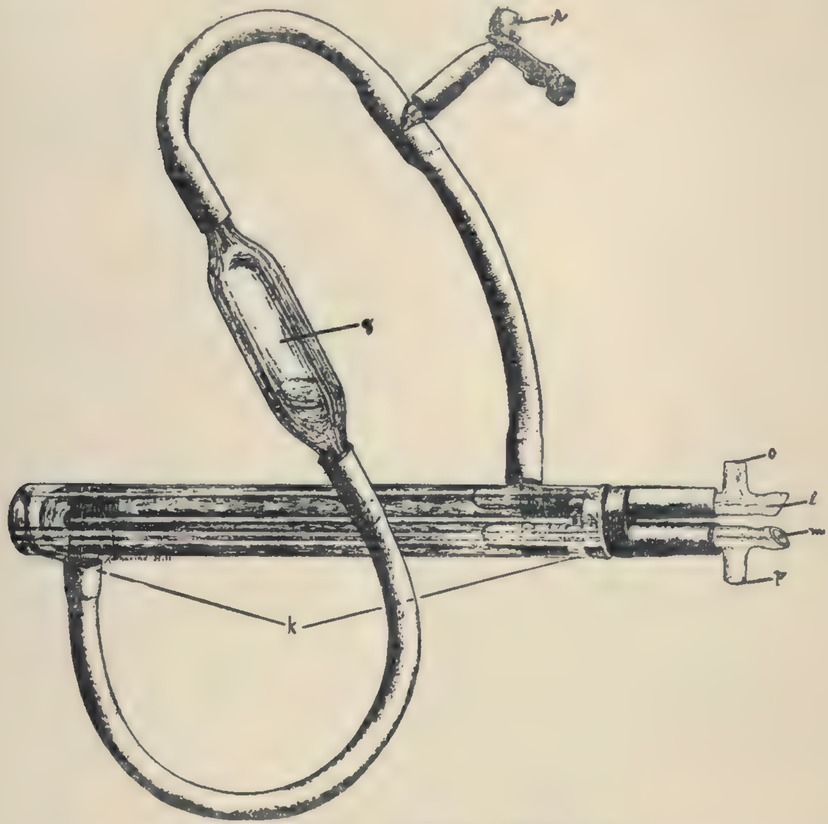
CONDITION OF SUGAR IN THE BLOOD

Analyses of blood showed, in corroboration of other workers,[33] that the plasma contains most of the blood sugar, while the corpuscles contain little if any and by far too small an amount to have any bearing whatever on a sugar equilibrium in the dialyzer. The corpuscles, therefore, may be considered merely as so many pebbles causing solid displacement of the plasma. Thus, if dog's blood be considered as averaging 55% plasma, the sugar percentage expressed in terms of the plasma more nearly equals that of the dialysate, being, respectively, 0.211 and 0.232 in the former, and 0.221 and 0.196 in the latter experiment. But, as the plasma content of the blood varies under different conditions, a more accurate sugar determination of

[33] Allen: Studies Concerning Glycosuria and Diabetes, 1913, pp. 6-7.

plasma is made from plasma itself. Table 1 shows the typical results of such analyses.

A close study of the comparative concentrations in the plasma and the dialysate furnishes some interesting facts. It will be noticed that, in every case of dialysis to a sugar equilibrium, the sugar is always about 10% greater in the dialysate than in the plasma. At first the



Dialyzing Apparatus not Requiring Anticoagulants.

This apparatus is about ⅓ natural size. The ends *l* and *m* are attached to the blood vessels. *o* and *p* are used for joining the flushing apparatus. The movable bulb *q* is used to mix the dialysate in the jacket and the connection *r* is attached to a syringe which raises or lowers the air pressure in the jacket at will.

possibility of a slight loss of either free or combined sugar in protein precipitation was considered, but other methods of precipitation and control experiments showed that this could not account for the discrepancy. Besides, the difference, though small, is too constant a

factor to be explained satisfactorily by an element of chance or experimental error.

It is evident that plasma and a saline dialysate are not comparable fluids by weight, since the former contains from 8 to 10% of solids, and the latter about 1% of solids. To compare them, even on a volumetric basis, would also be inaccurate, since 100 gm. of dog plasma, having a specific gravity of about 1.03, occupies 97.1 c.c., and, having 8% of solids, contains about 92 gm. or c.c. of water. Thus, there is approximately a 5% solid displacement, principally colloids, of the plasma by volume. Since the 1% solids in the dialysate are mainly of small molecular structure, there is practically no resultant displacement; hence a 5% error is introduced in the volumetric comparisons

TABLE 1

SUGAR DIALYSIS OF NORMAL CIRCULATING BLOOD

Dog No.	Anesthetic Used	Dialysis (hr.)	Sugar in Urine*	Plasma		
				Amount (gm.)	H_2O Content (gm.)	Dextrose Average (gm.)
9	Morphin..................	3.0	++	25.0	23.0	0.0339
6	Morphin..................	5.0	++	26.0	23.9	0.0326
7	Morphin..................	6.0	++	29.5	27.1	0.0258
8	Ether.....................	4.5	0	20.6	19.0	0.0170
5	Morphin and ether.......	5.0	0	25.0	23.0	0.0184
13	Urethan..................	2.0	0	19.9	18.3	0.0300
10	Urethan and ether.......	3.5	0	19.9	18.3	0.0324
11	Urethan and ether.......	4.5	0	19.9	18.3	0.0305
12	Urethan and ether.......	1.0	0	19.9	18.3	0.0312

Blood Vessels Used: carotid artery and external jugular vein.
Protein Precipitants: acetic acid and sodium sulphate.
Water Content Of: plasma, 92 %; dialysate, 99 %.
* At the end of dialysis.

of plasma and dialysate fluids. But, when these are compared on a gravimetric basis with proper corrections made for the solids, the sugar percentages, in terms of the water content of the plasma and of the dialysate, show a striking approximation, as may be seen from a study of Table 1. The results are so evident that they can indicate only that the blood sugar is not in colloidal combination, but in a simple solution in the water of the plasma. A critical discussion of this is given in our original paper.

Having decided that the sugar of the blood exists in simple solution, the next question is:* Can the muscles and glands use the sugar in this state? If not, we must surmise some error in our work and conclusions.

* This part of the work was done 10 years previously and when we thought the blood sugar was in colloidal combination. Am. Jour. Physiol., 1908, Vol. 21, p. 334.

Ludwig[34] thought that oxidation took place in the blood. We now know that the blood sugar is oxidized by the form elements mainly of the muscles and glands and only in minute amount in the blood. No oxidation takes place in the serum other than that due to the weak alkaline solution. When the blood is laked, glycolysis is stopped. The corpuscles contain no sugar. All these facts are in keeping with the free condition of the blood sugar. That the oxidation takes place in the form elements, and that the free sugar can be directly oxidized is supported by many other facts. First, in fermentation by yeast there is no action outside the cell, no extracellular enzyme. This may be easily shown by adding yeast to a solution of dextrose, and when fermentation is progressing rapidly, filter the solution through an ordinary

TABLE 1—*Continued*

SUGAR DIALYSIS OF NORMAL CIRCULATING BLOOD

Dialysate				% Sugar in			
Mixture per Hr. (no.)	Amount (gm.)	H_2O Content (gm.)	Dextrose Average (gm.)	Plasma	Dialysate	Plasma H_2O	Dialysate H_2O
30	27.8	27.5	0.0387	0.135	0.139	0.147	0.141
30	25.0	24.7	0.0333	0.125	0.133	0.136	0.135
30	30.0	29.7	0.0298	0.088	0.099	0.096	0.100
30	30.0	29.7	0.0262	0.083	0.087	0.090	0.088
30	30.0	29.7	0.0246	0.073	0.082	0.080	0.083
500	20.0	19.8	0.0336	0.151	0.168	0.164	0.169
40	15.0	14.8	0.0262	0.163	0.175	0.177	0.177
40	20.0	19.8	0.0339	0.153	0.169	0.167	0.171
500	15.1	14.9	0.0261	0.157	0.173	0.170	0.175

filter paper. Filtration by straining out the yeast cells stops fermentation instantly. Again, blood flowing through tissues loses some of its sugar. The amount is small, but is increased by muscular contractions; in fact, this is the method used to free an animal of glycogen. By use of strychnin, tetanus, strong muscular contractions, or other means leading to extreme fatigue, the liver becomes glycogen-free. That the free sugar can be used in this way is shown by perfusing isolated organs as the heart or muscles. Years ago I[35] perfused the isolated hind legs of animals keeping one leg in each case for control, and while the perfusion was proceeding kept the muscles working by electric stimulation. The results show clearly a loss of sugar, apparently by direct utilization. This work was done when we believed that the blood sugar existed as a colloid. By more refined methods more exact figures may be obtained, but we think that the facts will remain essentially the same.

[34] Lusk: Science of Nutrition, 1909, p. 19.
[35] McGuigan: Am. Jour. Physiol., 1908, 21, p. 334.

The method used consisted in perfusing the organ under investigation with blood containing a known amount of sugar and determining the loss of sugar during the perfusion. Usually the hind leg of an animal was used and the other leg kept as a control. Account was taken of the amount of glycolysis that the blood would have undergone during the time of the perfusion, the changes in the glycogen content of the leg, the changes in the sugar content of the leg, and the loss of the sugar from the blood. While the perfusion lasted the leg was stimulated through its nerve with an electric current. The idea of this was to increase the amount of sugar oxidized.

During the perfusion we never found that there was any formation of glycogen. Apparently the power of glycogen formation is lost before the power to oxidize sugars. Only the monosaccharids were oxidized. When the leg failed to respond to electric stimulation, the power to oxidize the sugars was greatly reduced and soon lost. Apparently, then, the living protoplasm is the active agent. A few of the results are presented in Table 2.

TABLE 2
RESULTS OF PERFUSION TESTS

Weight of Leg Muscle (gm.)	Time of Perfusion (hr.)	Sugar	Amount Used in 1 Hour (mg.)
100	1	Dextrose	15
100	1	Levulose	25
100	1	Levulose	33
100	1	Galactose	31

The heart while contracting also uses sugar. This has been shown by Knowlton and Starling,[36] by Rhode[37] and by Locke and Rosenheim.[38] Camis,[39] however, claims that it may not have been the perfused sugar that was directly oxidized, but the stored glycogen of the heart itself. There seems little basis for such contention. Our own work shows that the sugar may be used directly by the contracting muscle. While this work should be repeated, we think it is essentially correct.

The sugars that are used directly are those that are directly fermentable by yeast. The products are the same in both cases, and I believe the mechanism is also the same. In each case the living cell is the active agent. This can be readily shown in the case of the yeast

[36] Knowlton and Starling, Proceedings of the Royal Society, 1912, 85, p. 218.
[37] Ztschr. f. physiol. Chem., 1910, 68, p. 181.
[38] Jour. Physiol., 1907, 36, p. 205.
[39] Ztschr. f. allg. Physiol., 1908, 8, p. 371.

by passing through ordinary filter paper a solution of sugar that is undergoing rapid fermentation. The filtrate at once ceases to evolve gas. It is true as Buchner[40] has shown, that when the yeast cell is ground up the filtered juice will still cause fermentation, but this fact has been much overestimated, and the time that such fermentation will proceed is very short and suggests that it is due to living particles of the cell protoplasm. Similarly, but more marked, is the depressing influence of disintegration of animal tissues on the oxidative properties. This, I think, was the cause of Cohnheim's failure to demonstrate the synergistic action of muscle and pancreas extracts on the oxidation of glucose. There can be no doubt about the interrelated action of the pancreas and muscle in the normal animal, but since it is the living cell that oxidizes glucose, or at least the enzymes in the living cell, we should not expect in all cases that the same action can be demonstrated when the cell is disintegrated. The conjecture, however, was legitimate when isolated enzymes were considered as the sole source of oxidation. The method of Knowlton and Starling on the contracting heart, or of Macleod on the eviscerated animal seems a better method of attacking this problem.

Since the greater part of the digested carbohydrate is changed to glycogen in the body and this again to glucose before utilization by the tissues, it is of interest to know that conditions modify glycogenolysis. As is well known, some agents increase the blood sugar while others reduce it. I wish only to mention a few of these which we have recently investigated. In the first place: What is the effect on the blood sugar of modifying the circulation through the liver? We[41] have studied the effects of (1) portal ligation, (2) hepatic ligation, (3) simultaneous ligation of both portal and hepatic, (4) hyperarterialization, (5) Eck's fistula, and (6) reversed Eck's fistula. The results are shown in the accompanying tables. Hyperarterialization of the liver was accomplished by first making an Eck's fistula and then turning an artery into the portal vein or its branches. The results were obtained from acute experiments of 1 hour's duration, and clearly show that ligation of the portal vein, or greatly increasing the arterial blood going through the liver are the only operations to cause any marked change in the blood sugar, and these changes are never sufficient to cause glycosuria. We hold, therefore, that no conceivable change in the circulation can be of much importance as a causation of diabetes,

[40] Chem. Ber., 30, p. 117, 1110, 2668; 31, 32 (1897-1898).
[41] McGuigan and Ross: Am. Jour. Physiol., 1916, 39, p. 480.

unless the change secondarily involves the pancreas or some other organ. It is well known that if circulatory changes involve the pancreas sufficiently to produce inflammation of that organ, glycosuria may result. Uncomplicated changes in the liver circulation, however, can be of only small import as a direct factor. This is of interest in view of the fact that Bernard thought piqûre acted to cause glycosuria by changing the liver circulation.[42] It is now known, however, that unless the suprarenals and liver are both intact, piqûre alone will not cause glycosuria.[43]

The averages of the results of modifying the circulation are given in Table 3.

TABLE 3

RESULTS OF MODIFYING THE CIRCULATION

Exper.	No.	Dextrose in Blood, %		Length of Time Ligated, (min.)	Actual Sugar Increase, %
		Before Ligation	After Ligation		
Portal ligation	8	0.088	0.145	59	0.057
Hepatic ligation	8	0.105	0.124	60	0.019
Portal and hepatic ligation	8	0.126	0.114	50	—0.012
Hyperarterialization	8	0.176	0.238	50	0.062
Hypervenosity	5	0.141	0.157	60	0.016

TABLE 4

SUMMARY

Exper.	Increase of Sugar Content: Difference in % Before and After Operation, %	Increase of Sugar Content Before Operation, %
Ligated portal	0.057	62
Ligated hepatic	0.019	18
Portal and hepatic	—0.012	— 9
Hyperarterialization	0.062	35
Hypervenosity	0.016	11

CONDITIONS REDUCING THE BLOOD SUGAR

Hypoglycemia has not been considered so important as hyperglycemia. The reason is apparent. Diabetes is so common and so fatal a disease that all phases of it have attracted attention. When, therefore, it was found that the blood sugar is usually increased and that

[42] Bernard: Lecons sur le système nerveux, 1858, 1, p. 487.
[43] Mayer: Compt. rend. Soc. de biol., 1908, 60, p. 1123. Kahn: Arch. f. d. ges Physiol. 1909, pp. 128, 519.

when it reaches a certain concentration it passes into the urine, the cause of the disease was thought to be closely associated with the blood. On the other hand, we know of no disease where hypoglycemia is considered so important as the hyperglycemia of diabetes. The methods which reduce the blood sugar are worthy of attention for the following reasons: (1) They may illuminate the process of normal sugar metabolism. (2) They may reveal something of value in treatment. While such possibilities exist, it must be confessed that all of the known methods of sugar reduction are brutal and of much more immediate injury to the animal than the most rapidly progressing hyperglycemia.[44]

The conditions which may cause a reduction of the normal sugar concentration of the blood are extreme exhaustion,[45] suprarenal insufficiency,[46] Addison's disease,[47] thyroid insufficiency,[48] poisoning by phosphorus[49] and hydrazine,[50] high section of the cord,[51] anaphylactic shock, intercurrent affections,[52] moribund states,[53] and the injection of foreign proteins and the hypodermic administration of phloridzin. The striking physiologic changes that result from the application of most of the methods are: low blood pressure, splanchnic dilation, depleted vitality, and, in larger doses, a moribund state. In none of them is there the remotest suggestion of anything that operates for the welfare of the organism. Various artificial hyperglycemias and glycosurias have been reported to be lessened by the administration of certain glandular extracts or salt solutions. Stenström[54] found that pituitrin lessened adrenalin hyperglycemia. Dresel[55] reports that extracts of the pituitary, thyroid, ovary, or pancreas when injected with epinephrin reduce the height of the hyperglycemia. Miculicich[56] found that hirudin inhibited, and Glaessner and Pick[57] found that pancreatic juice and

[44] The treatment of diabetes recently advocated by Allen, F. M. (Boston Med. and Surg. Jour., 1915, 172, pp. 693-730), apparently does not deserve this condemnation.
[45] Weiland, W.: Deutsch. Arch. f. klin. Med., 1907-1908, 92, p. 223.
[46] Mayer, A.: Compt. rend. Soc. de biol., 1908, 64, p. 219.
[47] Porges, O.: Ztschr. f. klin. Med., 1910, 69, p. 341; 1910, 70, p. 243.
[48] Cushing, H.: The Pituitary Body and Its Disorders, 1910, pp. 132, 262.
[49] Frank, E., and Isaac, S.: Arch. f. exper. Path. u. Pharmakol., 1911, 64, p. 274.
[50] Underhill, F. P.: Jour. Biol. Chem., 1911-1912, 10, p. 159.
[51] Falta, W., quoted by Cammidge, P. J.: Glycosuria and Allied Conditions, 1913, p. 144. Chauveau, A., and Kaufmann, M.: Compt. rend. Acad. d. sc., 1893, 116, pp. 298, 551, 613. Bernard, C.: Lecons sur la physiologie et la pathologie du système nerveux, 1858, 1, pp. 466, 482.
[52] Cammidge: Glycosuria and Allied Conditions, 1913, p. 180.
[53] Macleod, J. J. R.: Diabetes: Its Pathological Physiology, 1913, p. 58; Bock, C., and Hoffman, F. A.: Jahresb. f. Thierchem., 1874, 4, p. 440.
[54] Biochem. Ztschr., 1913-1914, 58, p. 472.
[55] Ztschr. f. exper. Path. u. Therap., 1914, 16, p. 365.
[56] Arch. f. exper. Path. u. Pharmakol., 1912, 69, p. 128.
[57] Ztschr. f. exper. Path. u. Therap., 1909, 6, p. 313.

Witte's peptone lessen epinephrin glycosuria. Bock and Hoffman[58] showed that salt glycosuria is lessened by the further action of the injected saline. It is now known that calcium chlorid will lessen salt glycosuria. Underhill[59] found that the glycosuria produced by morphin, pyridin, etc., is reduced by the free administration of oxygen. Other cases of the kind are reported by Allen.[60] It should be stated, however, that the whole subject is unsatisfactory and contradictory to such an extent that many substances are recorded by some to produce hyperglycemia or glycosuria, while according to others the same drug causes hypoglycemia. Phosphorus, salt solutions, and peptones are among such drugs. Also in most moribund states the blood sugar increases immediately before death.

In making blood transfusions from one normal animal to another we have noticed that there is a general tendency for the blood sugar to the recipient to fall. We have since found that this is a common result of the intravenous injection of proteins and especially of peptones, although Henderson and Underhill[61] have reported glycosuria following the injection of peptone. We cannot confirm their results, and look on the glycosuria they describe not as a peptone, but as either an ether glycosuria or as an exception to the regular peptone action. Similar exceptions may be seen in those cases in which peptone hastens rather than retards the coagulation of the blood.[62] The whole subject of the action of sera, organ extracts, and toxins on the sugar content of the blood is in an unsatisfactory state, and the action perhaps varies with conditions.

In our work we used Witte's peptone chiefly, but we obtained similar results with silk peptone and with gelatin; and in several cases of anaphylactic shock, which resembles peptone action, we found hypoglycemia.

For the study of peptone hypoglycemia we used dogs entirely. The number of animals used without anesthesia was 17. The average weight was 10.6 kilos and ranges 4-18.5 kilos. The average dose of peptone was 3.7 gm. and was given intravenously in about 20 c.c. of water. The average normal blood sugar content was 0.65%. In 2-5 hours after the injection of peptone the blood was again analyzed. On the average, the time was 3½ hours. The blood sugar by this time on

[58] Quoted by Reichert and Du Bois-Reymond: Arch. f. Anat. u. Wissensch. Med., 1871, 38, p. 550; Jahresb. f. Thierchem., 1874, 4, p. 435.
[59] Jour. Biol. Chem., 1905-1906, 1, p. 113.
[60] Studies Concerning Glycosuria and Diabetes, 1913, p. 855ff.
[61] Am. Jour. Physiol., 1911, 28, p. 280.
[62] Stewart: Manual of Physiology, Ed. 5, 1906, p. 47.

the average was reduced to about one-half the original content, or 38%. We found a great reduction also when an anesthetic was used. The cause of the reduction is not clear. Perhaps it is due to changed circulation through the liver, although this can scarcely be sustained by experiment. It may also be due to a paralysis of the normal mechanism of glycogenolysis. The liver still contains considerable quantities of glycogen. In 3 cases which we analyzed the glycogen content of the fresh liver was 0.45%, 1.91%, and 3.18%. The blood sugar in the last case was lower than in any of the others. It may be that there is a greater utilization of the sugar in the circulating blood and lessened glycogenolysis, but this we have not investigated. The most common changes after peptone injections are low blood pressure and the unsatisfactorily explained condition known as fatigue.

INTERMEDIATE CARBOHYDRATE METABOLISM

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INTRODUCTION

In 1842, F. Bidder observed that the metabolism as a whole comprised 2 circuits: a greater circuit beginning with the entrance of matter into the body from the outside world and ending with the return of this matter to the outside world; and a lesser, laid between the ends of the greater, this lesser circuit beginning and ending within the organism proper. In 1847, Bidder and Schmidt, alluding to this distinction (in their monograph on The Digestive Juices and Metabolism) employ the term 'Intermediarer Stoffeweschsel' to designate the transformations of matter within the organism proper. This, as Lusk has noted, would seem to have been the origin of the term. Since then it has been used by some in more restricted senses and applied particularly to the purely chemical processes which occur as intermediate steps in the synthesis, destruction, or transformations of proteins, fats, and carbohydrates, or other body substances. According to this usage, processes of absorption, secretion, and circulation or transport generally would be omitted from the study of intermediate metabolism, but owing to the intimate connections which exist between the physical and the chemical phenomena, the older usage is here preferred. During the past few years the staff of the Sprague Institute Clinical Laboratory, including E. J. Witzemann, W. D. Sansum and Russell M. Wilder, have carried out detailed studies of certain phases of this general problem with particular reference to the intermediate metabolism of the sugars. The phases studied have been selected with reference to their bearing on certain general views. To facilitate the discussion of this work and in order that it may not appear disconnected, it will be necessary to develop briefly the point of view from which it was undertaken.

It is assumed that the intermediate metabolism taken as a whole represents multiple separate chemical reactions or groups of reactions confined to certain places or media with provisions whereby certain material and energic reaction products separate out of each and are

carried among and into others, thereby bringing all of the separate chemical reactions into a sort of dynamic equilibrium. For purposes of study, it is convenient to recognize two metabolic spheres: a sphere of chemical changes, in which molecules are breaking down, rearranging, building up; and a physical sphere or sphere of transport, in which intact molecules singly or in clusters, are in transit between the sites of chemical change. A 3rd or energic sphere may, for the purposes of the moment, be omitted from discussion. The first two spheres imply matter existing in two corresponding states: that undergoing chemical changes consisting of smaller particles carrying an excess of positive or negative charges such as ions and ion-like residues in general, and that showing little chemical reactivity but greater physical motion — consisting in the main of larger and relatively nondissociated or saturated molecules and of clusters of two or more such molecules, these clusters ranging in size from molecular dimensions to those characteristic of colloid particles.

Anatomic counterparts for these spheres are sought in fundamental classes of media which constitute phases in the heterogeneous or colloid structure of protoplasm and body fluids generally, this being merely the application to the study of intermediate metabolism in higher animals of the precept of Bichat to "first isolate the fundamental tissues of which all organs are made up and study each no matter where it is found in order finally to understand the several organs in their special characterization," and in harmony with the viewpoint of the general physiologists made familiar through the work of such writers as Verworn, J. Loeb, Kühne, Weinland, A. P. Mathews, M. H. Fischer, Little, and others. A tendency in the special literature covering various aspects of the intermediate metabolism in higher animals is still to deal with special organs as things separate and distinct in accordance with which tendency the circulating media, especially the blood, might be considered as representative of the physical and the cells of the chemical sphere. The blood plasma is of course essentially a medium of transport in which chemical reactions are slow. The work of Michaelis and of McGuigan have shown specifically for glucose that this metabolite exists in the blood in a state of physical solution. The cells, on the other hand, are recognized as the chief sites of active chemical changes. But individual cells possess powers of absorption, secretion, and chemical correllation, and even in the blood plasma some chemical changes occur, wherefore it is preferable

to regard both plasma and cells as made up of the same fundamental types of media, but in different proportions like the fat and the watery phases in cream and skimmed milk, respectively.

If in the study of intermediate metabolism we deal with the fundamental media which constitute the phases of such systems, it is readily understandable how metabolites such as glucose, amino-acids, and others existing within the body may be distributed between such phases in definite proportions, how in one type of medium they may exist in a state of simple physical solution, and in another, encounter conditions (enzymes, catalysts, or what not) which will favor a high degree of chemical dissociation. Illustration is afforded by the well known behavior of fatty acid such as butyric acid, which when added to an emulsion of benzene and water, divides itself between the benzene and the water phases in accordance with laws which pertain to the partition of dissolved substances between 2 immiscible solvents. The butyric acid then exists in the benzene in simple physical solution as single molecules in dynamic equilibrium with clusters of 2 or more molecules, the twos predominating. While in the water the butyric acid exists as single molecules in dynamic equilibrium with hydrogen and butyrate ions. In the water the dissolved substance is sufficiently dissociated to enter into chemical reactions characteristic of acids, such as the turning of ordinary indicators, the liberation of CO_2 from sodium carbonate, etc., but in the benzene such reactions occur if at all only to a very minute extent. The degree of dissociation of the butyric acid in the water phase may of course be greatly influenced by the simultaneous presence there of other substances.

The study of intermediate metabolism resolves itself, therefore, into a study (1) of the chemical reactions that occur among metabolites when mixed together in different proportions in homogeneous media which favor a high degree of dissociation and chemical reactivity; (2) of the physical or physicochemical reactions which occur when they are mixed in physical solvents; and (3) of the modifications which occur when the physical and chemical solvents are in contact with one another as phases in an heterogeneous system. For the explanation of reactions of the 1st type, chemical dissociation and the laws of chemical equilibrium will be of the greatest service, for the 2d, the laws of molecules, and for the 2 taken together, the laws of equilibrium in heterogeneous systems. In the final analysis, all phenomena of intermediate metabolism must represent the working out of these underlying principles.

METHODS

The recognition of processes proceeding in accordance with these laws within the organism must necessarily depend on the successful application of the principles of quantitative chemistry to the study of various biologic reactions now known in a purely qualitative sense. Indispensable to the movement in this direction is the development of refined methods of urine, blood, and tissue analysis which has received such material advancement in this country through the efforts of Folin, Van Slyke, S. J. Benedict, Shaffer, McCrudden, and others. A further necessity consists in methods which will enable us not only to detect, but also to create at will, within living cells, different definitely related concentrations of selected substances and to maintain these concentrations sufficiently long to permit measurements of the rates at which different physiologic processes proceed under these conditions. Or by direct methods, control the rates at which molecules of experimental substances enter the tissues.

When dealing with simpler marine forms definite concentrations of selected substances may be created within the cells by adding known quantities to the sea water surrounding them, and to maintain these concentrations it is only necessary to make the volume of water sufficiently large in proportion to the mass of the cells employed. In the higher animals the sea water has its counterpart in the circulating media, and to produce definite concentration of a given substance in the cells it may be made to assume a certain concentration in the blood. But since the ratio of the blood volume to the cell mass is small, in order to maintain a uniform blood concentration, the substance must be added continuously to the blood exactly as fast as it disappears into or through the cells. Methods of administration in which the substance must be absorbed from the alimentary tract or a subcutaneous, intramuscular, intraperitoneal, or other local injection site, prior to entering the general circulation, are open to the objection that absorption rates vary with many factors which are not subject to experimental control, and but sluggishly and within limits, to those which are. An exception should be made of intrapulmonary administrations. Owing to the expense of absorbing surface presented by the alveoli and the great perfection which has been attained in the development of respiration methods, it is exactly in this field that most progress has been made in the study of quantitative aspects of intermediate metabolism, and it is to such methods that the pharmacology of the inhala-

tion anesthetics owes its distinctive character. But only gaseous and volatile substances are susceptible of administration by inhalation. The majority must be administered in solution and the practical problem then resolves itself into one of ways and means for making direct intravenous injections at predetermined rates and of sustaining them uniformly for long periods of time.

A number of writers have devised apparatus for this purpose, but with the exception of a motor-driven quantitative pump described by Friedenthal, and exhibited at the International Congress of Physiologists at Gröningen, in 1913, none would appear to have embodied the qualifications necessary for work of the type under consideration. Nor am I aware of the existence in the literature of descriptions of experiments which would indicate that intravenous injections have been carried out with any type of apparatus at exact rates for periods of time exceeding 3 or 4 hours. During the past 2 years machines have been developed and used by the staff of our laboratory by means of which direct intravenous injections have been given to dogs and rabbits at predetermined uniform rates for 4 to 20 hours, and to men for as long as 5 hours. Earlier models have been demonstrated from time to time, the cut illustrating a newer and more satisfactory instrument. It consists of a graduated glass barrel with a metal piston, the nozzle connecting with a metal block in which is housed a metal valve constructed on the principle of a 2-way stopcock. A universal 20-horse-power motor provided with a true and heavy solid metal fly wheel actuates a worm which turns a driving wheel. The motion of the wheel is imparted by a cam and cam shaft to the valve in front of the glass pump barrel and by a separate motion to the piston itself, so that as the piston descends into the barrel, the contents are forced out through 1 opening, and as it returns, fluid is sucked into the barrel through a tube leading from a graduated reservoir. A link motion permits an adjustment of the length of the piston stroke to correspond with any desired fraction of the length of the pump barrel, and the number of strokes per minute is susceptible of delicate control by the rheostat. Either the coarse or fine adjustment is made without interrupting an experiment. Fluids of any viscosity from that of water to that of citrated blood or 100% glucose solutions are easily handled. With a uniform source of electric supply, one may deliver in an hour any chosen volume of fluid from 10 c.c. to 5 liters with an error of only a few tenths of a cubic centimeter. Since the entire action is positive,

the rate of delivery may be gauged at any moment by the number of revolutions of the driving wheel as well as from buret readings. This makes possible automatic speed indication. The power and momentum are such that the delivery rate varies inappreciably with changes of intravascular pressure; if the needle or cannula is intentionally occluded, the rubber tubing which connects the needle and pump will burst before the rate of the pump is greatly affected. All parts which come in contact with the fluid are easily detached for sterilization.

In experiments with dogs, the animals have lain on a board cushioned in blankets with a small cannula inserted into a suitable leg or abdominal vein, under novocain, a catheter in the bladder, and no general anesthesia. Great care has been taken to avoid pain and emotion, and the subjects as a rule have remained quiet and frequently dozing throughout the experiments, thereby eliminating nonphysiologic conditions. Experiments in which such conditions were not attained were considered unreliable. A check on the water balance suggested by Sansum, consists in allowing the animal board to rest constantly on scales, so that losses or gains of a few grams in bodyweight become visible through movements of the beam and susceptible of correction if desired, by providing a 2nd pump to discharge water into the delivery tube from the main pump, the 2nd pump idling except when required.

This method has been applied to the effects of different sugars when introduced into the blood stream at different rates, of a number of substances which are regarded as probable or possible intermediates in the metabolism of carbohydrates, fats, and protein, and also to a number of salts, both alone and in conjunction with the sugars, etc. I allude here chiefly to the experiments which bear most directly on the subject of intermediate carbohydrate metabolism.

EXISTENCE OF GLUCOSE IN TWO STATES OR PHASES

When d-glucose in gram molecular, or 18% aqueous solutions is administered to normal resting dogs by a peripheral vein at rates below 0.8 gm. per kilogram of body weight per hour, no glycosuria results, even when the administration is continued for hours; but when the rate of administration is increased to 0.9 gm. per kilogram per hour, glycosuria almost always develops within 30 minutes, the critical rate lying as a rule close to 0.85 gm. per kilogram per hour. This figure corresponds closely with that fixed by Blumenthal, who employed

repeated single injections to determine the intravenous tolerance limit for glucose and also with the figures obtained by Wilder, using the present method on human subjects. Thus a man weighing 70 kg. may receive glucose by vein at a rate of 56 gm. per hour without glycosuria which would imply, if the rate were maintained, the introduction of glucose sufficient to liberate 5376 calories per day, a point of some practical interest in the study of intravenous nutrition. But in the present connection the chief points are (1) that the glucose, when given even by peripheral veins, without passing through the liver first, does not lead to glycosuria, even when the rate of injection is such that the calories would suffice to cover twice over the total heat loss from the body under the conditions of the experiment prior to the beginning of the injection; (2) that with intravenous injections of glucose at rates below those which produce glycosuria, there is no increase in the urinary output of water. In fact, Sansum and Wilder have observed that when a human patient is kept quietly in bed with a uniform hourly supply of water, the hourly voiding of urine may be kept quite uniform, and when such patients receive subtolerant doses of glucose by vein in such a way that the total hourly water supply remains unchanged, the rate of urination is as a rule diminished during the period of glucose administration rather than increased. This phenomenon of antidiuresis is not less striking than that which occurs when glucose is given by mouth or subcutaneously, as described by Lusk, Fischer and Wishart, Allen, and others.

When d-glucose is given at rate of 0.9 gm. per kilogram per hour, under conditions otherwise the same, glycosuria develops and then ordinarily diuresis. This effect of intravenous glucose injection has long been known, having been studied especially by Doyon and Dufourt, Pavy, and later several others. When the rate of administration of glucose by vein is maintained uniformly hour after hour, with suitable provisions for the maintenance of the water balance as previously described, the rate of glucose excretion rises from hour to hour in a curve, the abruptness of which can be made to vary with factors under experimental control. Ultimately after 3 to 6 or more hours, depending on circumstances, the rate of glucose excretion becomes virtually constant, the curve then striking a plateau. Once such a level is reached, the rate of the hourly urinary excretion of glucose to the hourly intravenous supply becomes virtually constant. When the injection rate is below 0.85 gm. per kilogram per hour, the ratio of intake to output

approaches zero. With an injection rate of 1.8 gm. per kilogram per hour about 2% of the intake is likely to be excreted once constancy is attained. As the rate of injection is increased, the percentage excreted rises until when the injection is at the rate of some 3.6 gm. per kilogram per hour, the rate of excretion may average 35-40% of the intake rate. What absolute percentage of the 3.6 gm. is excreted will depend on a variety of conditions such as the water, salt, acid, and alkali balances, but especially the water balance. Gilbert and Carnot have held on the basis of large single injections that the ratio of the output to the intake becomes constant at or near 44% with doses exceeding a certain size, and Kleiner recovered on an average 60% of the glucose injected in a certain set of experiments. These higher ratios represent comparisons between total quantities of glucose injected and excreted from the beginning to the ending of waves of injection and excretion, respectively. The 35-40% excretions to which I refer are based on comparisons between uniformly maintained injection and elimination velocities enduring for 3-12 hours or more, the total quantity of glucose injected per hour being varied by varying the volume of the standard glucose solution injected. Naturally, however, the greater the absolute weight of the glucose administered, the greater is the absolute quantity which escapes unchanged in the urine and the greater the volume of water carried with it. As larger and larger volumes of 18% glucose solution are injected, a time comes when the water in the solution itself is not sufficient to counterbalance the rate of diuresis. Extra water is then drawn from the tissues and more water must be superadded from the auxiliary pump if we are to maintain a constant body weight and uniform sugar concentration in the blood and cells. Working with normally nourished healthy animals and 18-20% glucose solutions, and maintaining the water balance at whatever level is found at the start of the experiment, the 35-40% excretion occurs with remarkable frequency. By using more concentrated sugar solutions, allowing the dogs to become partly dehydrated and then maintaining the lower water level, higher percentage excretions of glucose may be obtained. But whatever absolute percentage of the 3.6 gm. or more of glucose per kilogram per hour given by vein is excreted in the urine, the same animal under otherwise similar conditions will excrete almost exactly the same percentage of the injected sugar when the rate is 3.6, 4.5, 5.4, 6.3, and 7.2 or any intermediate number of grams per kilogram per hour. These experiments indicate that when glucose is made to enter

the organism uniformly at a rate exceeding a certain minimum, a definite proportion of it constantly and permanently disappears, and the remainder as constantly escapes in the urine unchanged. One fraction suffers a chemical fate, the other a physical fate. Under the experimental conditions described, out of each 10 molecules of glucose which enter the body, we may say roughly 6 suffer a chemical fate and 4 a physical fate, no matter how many are given.

The explanation suggested is that glucose within the body exists in 2 forms, (1) as nondissociated molecules, (2) as unsaturated residues formed by the chemical dissociation of molecules, the 2 tending to be in equilibrium with one another as is the case with glucose in simple aqueous solutions as shown by the studies of Cohen, Mathews, Michaelis, and Nef. The constant ratios observed are not considered indicative of a relationship prevailing between the molecules and ions in chemical equilibrium in any single homogeneous medium, however, but a relationship prevailing in the body, taken as a whole, in which glucose is distributed between the phases of an heterogeneous system in one of which it is highly dissociated, whereas in the other it is dissociated only to a minute degree. The 2 fractions are adapted for separate consideration, and we may first allude to certain points of interest in the behavior of the nondissociated glucose molecules, or glucose in the physical sphere.

GLUCOSE IN PHYSICAL SPHERE

When glucose is given by vein to complete depancreatized dogs, the ratio of the injection rate to the output rate approaches unity. The same applies when lactose and many inorganic salts are given in health. In this situation all, or virtually all, of the injected glucose fails of dissociation, and we have purely the effects of the molecules. It would not appear, however, that there is any essential difference in the physical effects which are produced by administering glucose to a diabetic at a rate exceeding the tolerance rate by a certain definite margin and by administering glucose to a normal dog at a rate sufficient to cause the same rate of glycosuria, although it has been noticed in a long series of experiments with normal animals that the maximum urinary sugar concentration has been between 8 and 9%, whereas higher percentages than this are known to occur in diabetes mellitus (12 and 13%) and in phlordizin diabetes. In an 8.5% solution of glucose in pure water, the ratio of glucose molecules to water molecules is roughly

1 : 100. Something less than 100 would appear to be the minimum number of water molecules which must pass out of the body with 1 glucose molecule in experiments of the present type. If an unlimited supply of water is available, the urinary sugar concentration is always lower than this. But there is also apparently an upper limit to the number of molecules of water whose passage through the body will be hastened by the presence of glucose molecules. The possibility is, therefore, presented of fixing the maximum and minimum quantities of water which may accompany a molecule of glucose into the urine, and the question arises as to whether these maximum and minimum glucose water ratios correspond to different hydrates of glucose. In this connection work has been carried out with other substances, such as lactose and inorganic salts in the attempt to establish their diuretic coefficients with sufficient accuracy to arrange them in a numerical scale and to ascertain in particular whether the diuretic power of a substance is proportional to the electric charge on the molecule and the ability of the molecule to hydrate itself. Certainly isosmotic solutions of glucose, lactose, potassium acetate, citrate, and other salts are far from being isodiuretic. Their diuretic power, according to Fischer, parallels in a general way their ability to make protein gels give up water, and Hofmeister originally attributed the separation of water from protein gels under the influence of salts, to the tendency of the salt to hydrate itself. E. J. Witzemann points out a suggestive parallel between the observed diuretic powers of certain salts and their ability to change the percentages of ethylacetate, alcohol, acetic acid, and water in this well known equilibrium in a manner which has been explained by the Italian chemists as due to the tying up of water molecules in the form of hydrates of the salts, thereby affecting the equilibrium as though water had been abstracted.

Concerning the laws of glucose excretion and the relationships which prevail between the urinary and the blood glucose, the present technic enables one to maintain a constant blood sugar concentration, a constant urinary sugar concentration, or a constant total excretion rate, while other factors are varied. Ambard's laws have been tested in this way.

The most striking effects arising from glucose molecules are connected with the shifting of water. If glycosuria is maintained at a high rate by a correspondingly high injection rate, and if water is provided to the limit which can be carried away per hour, great volumes of fluid can be passed through the body. A certain dog

excreted for 8 consecutive hours an hourly average of 600 c.c. per 10 kg. of body weight, a rate of diuresis which for a man of average weight would correspond to 4800 c.c. per hour. Attempts have been made to apply this principle to the treatment of experimental poisonings with heavy metals, chloral, diphtheria toxin, etc. The results of this histolavage have been suggestive in the case of chloral, but disappointing in the case of heavy metals and diphtheria toxins. A good cardiovascular system and a sufficiently permeable kidney are prerequisite for success. During the first few hours of such diuresis there is a heavy washing out of chlorids and urea, after which the hourly excretion of these substances falls to a level. The impression which would seem to prevail in the literature that intravenous injections of glucose increase protein catabolism is doubtless based on observations of this initial flushing out in experiments which have not been continued long enough to see the end of the process.

If during a high rate of glucose injection the water lost in the urine is not wholly replaced, the animal loses weight, and when the weight loss reaches a certain grade, which will vary somewhat depending on the water level at the beginning of the experiment, the animal begins to grow restless and increases the depth and frequency of his respirations. If at this stage the water deficit is restored by accelerating slightly the rate of the auxiliary pump, these symptoms disappear and it is remarkable how sensitive the organism is to slight variations of the water balance above and below a certain critical level. After the appearance of some restlessness and hyperpnea, if dehydration is permitted to proceed, the animal shakes and shows every sign of having chills, and at about this time or soon after the temperature rises. It is possible to produce definite rigors and fever as high as 125 F. in dogs, but unless dehydration is carried too far, chills, fever, shaking and hyperpnea all disappear when the body weight is brought back to the proper level by adding water. Exactly similar phenomena may be produced with other diuretics besides glucose, and in the employment of glucose solution by vein in the clinic for the intentional dehydration of persons with glaucomatous eyes, chills, and fever as high as 102 F. have been seen. Emphasis is laid on the water balance in this connection. The fever can be made to appear and disappear by changing the water level.

Concerning the clinical value of intravenous injections of glucose at diuretic rates with intentional dehydrations of the body, it might be

supposed, a priori, that this method would have value in the reduction of certain forms of edema, fluid accumulations in body cavities, etc., and cautious experiments have been made in a variety of clinical conditions to test this possibility. In cardiac edemas the procedure would appear to be irrational and injurious. When glucose is injected into the blood, it passes into the tissues with great rapidity. Meltzer and Kleiner have demonstrated how quickly glucose leaves the blood stream following its introduction into the veins even after death. Once in the tissues in increased concentration, glucose molecules cause there a shrinkage of the colloids with separation of water, explainable perhaps on the basis suggested by Hofmeister that the glucose molecules hydrate themselves at the expense of the colloids. But however the effect may be explained, it is as Fischer has demonstrated, a phenomenon quite analagous to that which we see when glucose is added in sufficient concentrations to protein gels in vitro. Before this water which is freed from the colloid combinations to become a glucose solution can leave the body, it must first enter the blood stream and be transported to the kidneys. A great increase in blood volume and blood pressure results. The water which the tired and flagging heart has given the tissues to hold while it rests is again saddled on it. There may be some increased diuresis, but only at the cost of increased cardiac effort with no compensatory advantage. The same general principles should apply to the use of any intravenously administered diuretics such as salts, the diuretic effects of which are ascribable to the same basic mechanism. Such methods are also contraindicated, according to our observations, when the kidney is so badly and irreversibly changed that even though the heart is strong the kidney presents an insurmountable barrier in the passage of the water separated from the colloid combination by the sugar. On the other hand, for the persons having adequate cardiorenal mechanisms and localized edemas, the situation is different. In a certain case of glaucoma we have reduced the intraocular tension 3 times from about 57 to normal limits inside of an hour and a half, which effect is analogous to the spontaneous production of the 'soft eyeball' of diabetes by the same dehydrating effect of dissociated glucose molecules. Riessmann has recently studied this condition from the clinical standpoint. Such methods may also be used successfully to start diuresis in certain cases of acute anuria in which the kidneys are strangled by swelling under the capsules — the same type of cases in which decapsulation may be

followed by a restoration of function. In such cases the beneficial effects lasting after the injection has ended would seem to be due, as Fischer already has held, to the relief of pressure, the coincident reestablishment of the oxygen supply caused by improvement of the blood flow through the part and the resultant diminution of asphyxial acid accumulations.

THE CHEMICAL PHASE

We may now return to the consideration of the fraction of glucose which during constant intravenous injections at high rates disappears and suffers chemical changes. Metabolism experiments carried out in conjunction with Dr. Walter M. Boothby and Miss Irene Sanford in the respiration laboratory of the Peter Bent Brigham Hospital, Boston, for the privilege of which I take pleasure in thanking Dr. Harvey B. Cushing, showed that in dogs receiving 3.6 gm. of glucose per kilogram per hour — of which about 2.4 gm. disappeared — not over 0.6 gm. gave evidence of actual oxidation. The nonprotein respiratory quotient remained close to 1.0 and the assumption was that most of the remaining 1.8 gm. was polymerized under the conditions of the experiments. By feeding experiments, Lusk had shown that the administration of increasing quantities of glucose caused increases of the total metabolism up to a certain point, after which the feeding of more sugar caused no further increase. The question arises as to whether this indicates a limit to the rate at which glucose can be absorbed, or, as he suggests, an actual upper limit to the amount which can be oxidized, no matter how great a sugar concentration is produced in the cells. Although the rate of glucose oxidation indicated by the data of Boothby and Sanford is somewhat above that obtained by Lusk and by Grafe after feedings of glucose, the discrepancy would seem remarkably slight when it is recalled that glucose when introduced into the blood at the rate of 3.6 gm. per kilogram per hour in 18% solution may produce and maintain a 0.55-0.66% blood sugar concentration with a steady and intense glycosuria of 12-14 gm. per 10 kilograms hourly, whereas glucose given by mouth can only cause an hyperglycemia in the peripheral blood a trifle above or below the normal threshhold value. This would support Lusk's interpretation — although further studies in metabolism are needed — on animals in which the cells and blood sugar concentrations are maintained at levels higher than can be attained by absorption methods of administration and higher than these just described. Until such studies are made, discussions of possible

numerical relationships between the fractions of glucose which are oxidized, reduced, and polymerized, respectively, during the maintenance of different uniform blood sugar concentrations under standardized normal conditions, as well as the factors which might be expected to change such relationships, would be largely speculative. It would appear, however, that normally the rate of glucose oxidation varies within a comparatively small range, while the relationship between the rate at which glucose is precipitated in the form of glycogen and the rate at which it is excreted unchanged may be more nearly reciprocal. The studies of McLeod bear interestingly on these points.

On questions of the mechanism of glucose polymerization, reduction, and oxidation, and the intermediate steps which occur in these processes, a vast amount of study has been bestowed by many workers, particularly on the question of oxidation. For various reasons it has been inferred that the breakdown of glucose in the body leads to the formation of a chain of smaller molecules of more or less stable and well defined substances, such as glyceric aldehyd, lactic acid, pyruvic acid, methylglyoxal, etc. With the exception of lactic acid, which under asphyxial conditions may accumulate to the extent of 0.5% and more in the muscles and to smaller degrees in other tissues, few if any of these supposed intermediates have been demonstrated within normal tissues or blood, nor has there been any direct method of proving whether or not a suspected substance is actually formed during the oxidation of glucose in the body.

We should not expect that any intermediate which might be formed during the normal oxidation of glucose to carbon dioxid and water will ever be found in appreciable quantities in the blood plasma or urine. The blood plasma is made up, as stated before, almost wholly of a non-ionizing or physical solvent whose principal function it is to transport molecules of food to the various sites of chemical change and to carry molecules of end products from those sites. An end product of one reaction mixture may indeed be food for another, in which case it might be referred to as a physical intermediate or an intermediate in a polyphase reaction. Well defined molecular substances such as glycin, alanin, or glucose itself are examples of such physical intermediates in the building up, oxidative breakdown, or transformation of the more complex body substances such as proteins, polypeptids, glycogen, and polysaccharids, respectively. Many such reactions as the formation of glycogen from protein are scarcely capable of duplication in vitro in

any one homogeneous medium. Hence for their fulfilment, substance must pass from one chemical reaction mixture to another through what we have called the physical sphere, or sphere of transport, in which a molecular state of matter prevails. But the oxidation of glucose to carbon dioxid and water can be carried out easily in a simple aqueous solution of any ordinary alkali, such as caustic soda, by means of air, hydrogen peroxid, or other oxidizing agent, and there is no necessity for assuming that in the oxidation of glucose in vivo certain intermediate products are formed which cannot be oxidized further at the site of their origin, but must diffuse out into the physical phase in the form of molecules for transport elsewhere, and so be found in the blood plasms and similar media. In the normal oxidation of glucose in the body the chief substances of this type are carbon dioxid and water. All intermediate steps between glucose and carbon dioxid and water might be expected to take place in one type of medium, a medium in which the prevailing state of matter is ionic or ion-like. Ions as such are not known to be capable of diffusing out of the medium on which existence depends. If molecules were formed in such a medium and failed to undergo a high degree of dissociation they should accumulate there in considerable concentration and so necessarily diffuse out into the physical phase. They would then be end products of the particular reaction, not true chemical intermediates. The blood plasma as a fluid consisting predominantly of a physical type of media should then contain such products in demonstrable quantities.

This hypothesis can be subjected to experimental test as follows: As stated above, glucose can be made to oxidize in the body at the rate of 0.6 gm. per kilogram per hour. Glucose burning at this rate in any specified way would necessarily produce ashes or intermediates at a definitely calculable rate. We may take any proposed scheme of glucose oxidation, figure the rate at which each intermediate would have to be formed according to this scheme, and then administer each of these intermediates by vein at this rate and see whether or not the effects are compatible or incompatible with the hypothesis. It has been proposed that in the normal oxidative breakdown of glucose in the body the great preponderance of the 6 carbon glucose molecules first split into 2 molecules of the 3 carbon sugar glyceric aldehyd. This implies that 0.6 gm. of glucose burning per hour per kilogram of body weight introduces into the body 0.6 gm. of this triose per hour. But experiments show that glyceric aldehyd administered at such a rate is

decidedly and characteristically toxic, even fatally so. Even at one-sixth of this rate glyceric aldehyd injections cause unchanged glyceric aldehyd to appear in the urine. Neither of these effects is seen when glucose itself is given at any rate up to 7.2 gm. per kilogram per hour. Therefore, if any molecules of glyceric aldehyd are formed in the oxidative breakdown of glucose, the rate of formation is so small that the glyceric aldehyd concentration produced in the tissues is below that which results from administering glyceric aldehyd at only one-sixth of the rate at which Embden's hypothesis would demand. Recent experiments of a different nature by von Fürth have also cast doubt on the validity of the idea that glyceric aldehyd can constitute a chief normal intermediate in the glucose catabolism. Quite analogous discrepancies are found when in place of glyceric aldehyd we substitute lactic acid, pyruvic acid, and each of several other molecular substances which are considered as probable intermediates, and the conclusion would seem necessary that none of these substances is a chief intermediate in the commonly accepted sense. No suggestion is made that these substances may not, however, be molecular forms closely related to the true intermediate substances. They may represent, as Otto Neubauer put it, the nearest separable ('fassbare') products.

Some relaxation of the stiffness of my conceptions of the oxidative breakdown of glucose might be desired. Instead of conceiving well defined molecular substances as obligatory forms which must be passed through in succession, like water flowing from one fixed basin to another in a fountain, we might rather think of glucose catabolism as a swiftly running, natural river, in the main channels of which there are no forms more fixed than the changing eddies. Molecules might then be conceived as the quieter bayous and backsets away from the principal channels.

DISCUSSION

R. G. Pearce: The great advancement which physiologic and organic chemistry have made in the past decade have opened up many new fields for the experimental physiologist who is interested in carbohydrate metabolism, and I feel sure that the further advancement of our knowledge in this subject lies in a more complete application of physicochemical laws, similar to those which Professor Stieglitz suggested this evening.

The fact that the physicochemical processes of ionization may play a part in the oxidation of carbohydrate in the body, as well as the enzymes, is most important.

During the past 8 years, Dr. Macleod and I have done considerable work in the Laboratory of Physiology of Western Reserve University, Cleveland, on the

glycogenic function of the liver, and its relationship to hyperglycemia and glycosuria.

A number of years ago Ellias reported that a marked hyperglycemia and glycosuria followed the intravenous injection of acid into a dog. He concluded that acid influenced the breaking-down of glycogen in the body. With this in mind, Dr. Macleod and I tested the rate of glycogen synthesis in the liver during the injection of glücose solution into the superior mesenteric vein. This work, which Dr. Macleod has completed since I came to Chicago, has demonstrated that the presence of acid in the perfused fluid inhibits, and the presence of alkali favors glycogenesis. This would indicate that the process of glycogen synthesis is dependent on electrolytic phenomena, such as Professor Stieglitz has called attention to.

The problem of carbohydrate metabolism is tied up so intimately with the problem of diabetes, that anything in connection with diabetes is of interest. It has been mentioned that Dobson had to share the honor for the discovery of sugar in the urine in diabetes with others. We usually have to share the honor of discovering anything with others. I am informed von Mering and Minkowski owe their discovery of the relationship of the pancreas to diabetes to the observation of their laboratory servant. It seems that they were interested in the digestive function of the pancreas, and during the course of their investigation removed the pancreas from several dogs. After some time, during which they failed to visit the laboratory, they inquired of their laboratory servant concerning the health of the dogs. He informed them that the last one had just died the same morning. He also mentioned that the dogs had been very hungry and thirsty, and had passed a large amount of urine, which attracted the bees. Minkowski, on testing the urine remaining in the bladder, discovered the presence of sugar, and also the relationship of the pancreas to carbohydrate metabolism.

The intermediary metabolism of the carbohydrates is an interesting subject. The work of Dr. Woodyatt in connection with the constant intravenous injection of substances is epoch-making. Through its use he has been able to test the various theories concerning possible intermediary substances found in the metabolism of glucose, and I think it offers a wide field of usefulness for the future. I should like to ask him what he thinks of Embden's work on the relationship of phosphoric acid and glucose metabolism.

The hypoglycemia following peptone shock, which Professor McGuigan discovered, reminds me of some experiments which Mr. Zucker and I did 2 years ago in an attempt to determine the effect of peptone on the blood flow through the liver. The liver of a small dog was removed and a cannula was quickly inserted into the portal vein. Through this cannula was perfused, under constant pressure, normal citrate blood and citrated blood obtained from an animal in peptone shock. The perfusion of the latter was usually accompanied by a great decrease in the rate of flow. I wonder if the hypoglycemia observed by Professor McGuigan in peptone poisoning is due to similar interference in the circulation of the liver.

S. STROUSE: It seems to me that the contention that blood sugar is free, and is used by the tissues and the glands in a free state, is pretty definitely proved by Dr. McGuigan's experiments. Recently Meyer made in-vitro experiments on the action of tissues on sugars, and his experiments seem to prove the point made by Dr. McGuigan. In the Michael Reese Hospital we have a method that has made the study of blood sugar practically a clinical procedure. We need only 0.5 c.c. of blood, which, of course, will allow continued researches on the same patient, for instance, in diabetes, to get the result of treatment. It also affords

opportunity for continued study of animals without any possibility of interfering by psychic or physical disturbance with the sugar content, so that the method at present is both an experimental and clinical procedure.

I was interested, in looking over my records, to find that there was only 1 case of hypoglycemia which I have encountered clinically, and that was in a young boy who had what looked like a Froehlich's syndrome, and who, 2 hours after a heavy dinner, to which was added 100 gm. of glycose, showed a figure of 0.02%. This was lower than any I had ever obtained in normal persons, even in a fasting condition early in the morning.

The question of hyperglycemia is so intimately bound up with the clinical study of diabetes and the treatment of diabetes that I take the opportunity of giving you some figures we have obtained. Formerly we were taught that 1 of the aims in the treatment of diabetes was to get the blood sugar to a normal level. In the work I have done so far I have found it practically impossible, except in the very mildest cases, to maintain a normal blood sugar level in a diabetic. In the cases of moderate severity the treatment, even by starvation, may reduce the blood sugar to normal for a short period, but the addition of even a small amount of carbohydrate to the diet will raise the blood sugar level above the normal level, although, as a rule, one may maintain a lower value than before treatment. The value of following this line of study is as yet unknown to us, especially from the standpoint of prognosis.

One point was brought out about the specific enzyme necessary for the oxidation of glucose in the body. The whole question of specific enzymes is creating great discussion now, on account of Abderhalden's work. Abderhalden has claimed to be able to immunize the body against sugars which it cannot use normally. Whether he has succeeded or not, I do not know, but others assert it is absolutely impossible by any means to make the human body capable of handling anything but the monosaccharids.

H. McGUIGAN: Just one point, namely: It has always been hard to explain why sugar passed out of the kidneys when it reached 0.3%, or thereabouts, and not before. Since we believe that all of the sugar of the blood is in a state of simple solution, it has been hard to explain why it does not pass through the kidney. After listening to Professor Stieglitz and Dr. Woodyatt, I can form a reasonable explanation why it does not pass out, and I think the others can also.

R. T. WOODYATT: With reference to Professor Stieglitz's suggestion about sodium chlorid: A solution that has excited comment consists of 0.3% sodium carbonate in 1.4% sodium chlorid. This can be perfused through animals or men in the same way, producing diuresis comparable to that shown. We have tried this for experimental mercuric chlorid poisoning, and it has seemed to have a somewhat better effect than glucose. But such a solution produces also catharsis simultaneously with the diuresis, so that the possible advantage might be explained by the increased excretion of mercury through the bowel, where a considerable amount of the heavy metals go. But neither with Fischer's nor any other solution has it been found possible to reestablish anything like a normal rate of urination relative to the volume injected. It seems possible that the mercuric chlorid no longer exists in the form of the free salt, but rather combined with the cell protoplasm, perhaps as an albuminate.

With reference to the question regarding Emden's work on phosphoric esters. I have not studied this in sufficient detail to express views as to how the phosphoric ester would act, but in any case this work would not be out of harmony with the fundamental principles that have been discussed.

ETIOLOGY OF THE EPIDEMIC ACUTE RESPIRATORY INFECTIONS COMMONLY CALLED INFLUENZA

George Mathers

November 7, 1916

Epidemics of acute respiratory infections have occurred at irregular intervals for centuries in various parts of the world, and their prevention has been one of the most formidable problems in preventive medicine. These infections, different from other epidemic diseases, seem least liable to modification by hygienic or geographic conditions, and at some time in its history almost every race of people has suffered from their ravages. During these visitations, recorded in centuries of medical history, the general mortality is greatly increased; the etiologic agent, independent of its own virulence, may increase the death rate by combining with preexisting diseases, or by lowering the resisting power of the person to such an extent that other more formidable infections gain a foothold and cannot be overcome. Furthermore, it is striking that, notwithstanding the wide diversity of conditions under which these great epidemics have occurred, the clinical manifestations of the disease have always been the same. Usually the symptoms are those of an acute infection of the upper respiratory tract, but occasionally of the intestinal tract, with a rapid course and characterized especially by a marked prostration of the patient. The complications are quite numerous, and probably represent the most important factor in determining the mortality of these diseases. Infections of the accessory nasal sinuses, lobar and lobular pneumonia, pleurisy, lymphadenitis and otitis media are common complications, while arthritis, pericarditis, abscesses, erysipelas, peritonitis, appendicitis, cholecystitis, illnesses diagnosed scarlet fever, and acute nephritis are frequently observed.

The pathologic anatomy of the disease is quite varied, and usually consists of the complicating morbid changes. Acute inflammation of the mucosa of the respiratory passages, varying grades and types of lobar and lobular pneumonia, generalized lymphadenopathy and infections of the various serous surfaces of the body may be mentioned as more or less typical of the pathologic anatomy of these infections.

Nothing can more forcibly indicate the definite character of the causative factor in these epidemic infections than this close similarity of symptoms and complications during several centuries and under such varying degrees of civilization. Whatever this factor may be, it must have a universal distribution and a most variable pathogenicity. Aside from a few observations on previous isolated epidemics, the most important bacteriologic work on these diseases was done during the great pandemic of 1889-1892. Notwithstanding the great number of observations during this time, however, no observer has satisfactorily proved that one species of bacteria is of primary importance in the causation of the disease. The larger group of investigators, including Weichselbaum, Newman, Ribbert, Finkler, Friedrich, Jaccoud, Gaucher, Bouchard, and others found streptococci, pneumococci and staphylococci in the sputum and postmortem material from cases of influenza, and regarded the disease as a streptococcus or a mixed streptococcus and pneumococcus infection. In 1892, however, Pfeiffer published his great work on influenza in which he described a small gram-negative hemoglobinophilic bacillus as the causative factor, and this work gained almost universal acceptance at this time. The previously described bacteria—streptococci, pneumococci, and staphylococci, because of their frequent presence in the sputum of normal persons, were henceforth considered as secondary invaders and of minor importance in the etiology of influenza. Pfeiffer isolated influenza bacilli from the sputum and bronchial tissues of persons suffering from the disease, but he was unable to find these organisms in the blood stream or satisfactorily to reproduce the disease in animals, although many attempts were made. Similar results were obtained by many of Pfeiffer's contemporaries. According to Pfeiffer, these gram-negative hemoglobinophilic bacilli cause true influenza, which he considered a local inflammation of the respiratory tract. Although these conclusions obtained wide acceptance for a time, except in France, recent investigators have failed to corroborate his findings, and the importance of this organism has been called into question. Davis and others have repeatedly found these bacilli in various diseases, such as whooping cough, tuberculosis, and chronic bronchitis, in which there is a mucous expectoration, and many other diseases, and except in influenzal meningitis these observers consider the influenza bacillus of no primary importance. Again this organism has not been found with any regularity associated with the epidemics of acute respiratory infections

since 1890. Whether or not Pfeiffer's bacillus was the causative factor in the great pandemic of 1890, there has been little evidence brought forward in recent years to support the view that it is of any great importance in the etiology of the disease.

During the winter of 1915-1916, the United States was visited by a severe epidemic of acute respiratory infections which resembled in every detail the great epidemic of 1890. This outbreak was apparently first noticed in the middle western states, and it spread rapidly over the entire country, taking a heavy toll of human life. December and January were the months in which these infections were most prevalent, and the epidemic had almost completely lost its impetus by March, 1916. During the height of this epidemic in Chicago, 61 cases of the disease were studied bacteriologically, and the results form the basis of this paper.

In all the cases the nasal discharge and sputum were examined, and in a few instances blood cultures were made. In 46 instances, hemolytic streptococci were found in predominating numbers, and in 6 of these cases these organisms were isolated from the nose and throat in pure culture. Green-producing streptococci were found in 30 instances with 1 pure culture, and pneumococci in 30 cases with 4 pure cultures. Staphylococci were isolated in 50 cases, Micrococcus catarrhalis in 6, and Freidländer's bacillus in 1 case. In only 1 instance was the influenza bacillus found, and then in small numbers. Anaerobic cultures were also made in the majority of cases, but there were no findings of any great interest. The rhinitis bacillus, which has been described by Tunnicliff in connection with acute rhinitis, was found in the nasal discharge in 2 cases, and fusiform bacilli were not uncommonly observed in these anaerobic cultures.

The majority of the patients were studied early in the course of the disease, and, in the earliest of these, hemolytic streptococci were almost constantly found, especially in the throat. These different strains of streptococci grew on standard blood agar plates as small round semitranslucent colonies of variable moisture surrounded by a clear zone of hemolysis 2-3 mm. in diameter. They were gram-positive, arranged in pairs and short chains, medium sized and slightly oblong, and occasionally faintly staining capsules were visible. They were highly virulent for rabbits, doses of 1 c.c. of a 24-hour broth culture usually causing multiple arthritis and death in 5-10 days.

The pneumococci isolated were usually in small numbers, and often

presented the characteristics of the organism found in the mouths of normal persons which Cole and his associates call Group 4 or the atypical type of pneumococci. The green-producing streptococci were also usually found in small numbers, and were in the instances studied relatively avirulent. In regard to the staphylococci found, it is interesting to note that many of the strains were hemolytic when first isolated.

In many instances the attacks of grip were followed by atypical pneumonias, and bacteriologic studies of material from these cases, both antemortem and postmortem, revealed the presence in predominating numbers of hemolytic streptococci in most instances. In no instance in which postmortem material was examined was the influenza bacillus found. In 9 cases blood cultures were made, 4 of which were positive, 3 yielding hemolytic streptococci and 1 pneumococci in pure culture.

The most significant findings in this work were the hemolytic streptococcus, which, when present, was usually in predominating numbers, and the almost complete absence of the influenza bacilli, although the disease simulated in every detail the so-called true influenza. The question of filtrable viruses cannot be excluded in such diseases, but in 3 early cases in which virus cultures were made no results were obtained. The results seem to indicate that the virulent hemolytic streptococcus must be considered as an important factor in the etiology of these 'grippal' diseases. Whether or not the infection is primarily a streptococcus infection cannot be determined; but, as the disease progresses, this organism rapidly becomes of paramount importance.

Throughout the literature on epidemic human respiratory infections there have been described coincident widespread epidemics of acute distempers among horses and occasionally other animals. These epidemics have been so frequently simultaneous that many of the earlier observers have described the clinical manifestations of the disease minutely. It is only necessary to say that the clinical picture, pathology and complications of the equine epidemic disease simulated closely epidemic respiratory infections in man.

The clinical symptoms are always the same. The onset is sudden with a chill and high fever, or with a profuse mucous nasal discharge which rapidly becomes purulent, and profound exhaustion. In exceptional cases, gastro-intestinal symptoms have been noted as premonitary manifestations. The course is rapid, and usually terminates

favorably unless serious complications intervene. The complications are, however, frequent, and determine the character of the prognosis. Pneumonia of a lobular type but in some instances lobar, pleuritis, empyema, abscesses, arthritis, acute nephritis, and conjunctivitis are the most common complications. The pathologic picture simulates that of human 'grippal' infections, and it may be said that the 2 infections are quite similar in epidemiology, clinical manifestations, pathology and complications.

Such an epidemic occurred among the horses of the United States during the winter of 1915-1916, and was at its height during the decline of the human epidemic, gradually abating with the advent of warmer weather. Great numbers of horses were attacked, and the disease spread rapidly along the various shipping routes to all the great concentration markets in the country. This epidemic was felt more severely in Chicago and New York, and in these cities thousands of horses suffered from the disease.

By the courtesy of Mr. A. G. Leonard, I had the opportunity to study this epidemic infection as it occurred in the Union Stock Yards veterinary hospitals in Chicago. Extensive bacteriologic observations were made on the nasal discharges and blood obtained during all stages of the disease, and on a large amount of fresh postmortem material. The technic used was similar to that used in the examination of material from human infections.

This work, which includes examinations of more than 100 horses sick or dead with the disease, yielded strikingly uniform results. Hemolytic streptococci have been isolated in pure or mixed culture from the nasal discharge before death, and from the infected tissues after death in almost all instances. In a large series of blood cultures taken at various stages in the course of the infection, hemolytic streptococci were found in pure culture in a large percentage of cases. Furthermore, these organisms have been isolated from pneumonic exudate obtained by lung puncture during life, infected joints, kidneys, and urine in acute nephritis, abscesses, iritis exudate, acute painful swellings on the extremities of infected horses, a condition simulating erythema nodosum in man, and infected lymph nodes during the course of the disease. Other organisms, such as staphylococci, green-producing streptococci, gram-negative bacilli and Bacillus subtilis, were found occasionally in the cultures from the nasal discharges. It is also

interesting to note that the tetanus bacillus was found in these cultures in a few instances.

The results which have been briefly outlined indicate that the hemolytic streptococcus was a factor of primary importance in the etiology of this epidemic infection in horses; but before this conclusion can be considered logical, other possibilities must be excluded. The question of filtrable virus being responsible for the infection must be considered. To obtain some information on this question, many culture and inoculation experiments have been carried out. The methods for the cultivation of viruses suggested by Noguchi and others were used, and Berkefeld filters were usually found of sufficient density to remove the bacteria. In 12 instances the mucous nasal discharges of horses in the 1st stage of the infection were suspended in sterile physiologic sodium chlorid solution and filtered through Berkefeld filters. This filtrate was cultured aerobically and anaerobically as well as sprayed into the nose of normal horses. In no instance did these culture or inoculation experiments yield any results which would indicate the presence of a filtrable virus. It is reasonable, therefore, to conclude that, using the known methods for identification of a virus, a virus is either not present in the nasal discharges of horses suffering from epidemic respiratory infections or it is not demonstrable.

Of 3 horses which were inoculated intranasally, however, with washed fresh cultures of hemolytic streptococci, 1 developed the typical acute infection 3 days after inoculation. This experimental infection ran an uncomplicated course and terminated in recovery in about 14 days. The other 2 horses developed a slight mucous nasal discharge following inoculation, but the general reaction did not justify the conclusion that they were suffering from the disease. Up to this time immunity reactions have been studied in only a few instances, and the results have been inconclusive.

The streptococcus isolated from the equine respiratory infections corresponds with the organism described by Hel, Schütz, Pfeiler, and others as the etiologic factor in pleuropneumonia in horses. The streptococci from human and equine sources, although similar in many characteristics, differ widely in pathogenicity, and seem to be highly parasitic for their specific hosts. The pathologic anatomy of the 2 epidemic respiratory diseases, human and equine, however, are quite analogous and typical of streptococcus infections.

When the observations just described are collated, some interesting

relationships become evident. The epidemic of acute respiratory infections occurring in the United States during the winter of 1915-1916 simulated in every characteristic the great epidemic of 1890. In a detailed bacteriologic examination of material from 61 instances of this disease, the influenza bacillus was found in only 1 case. On the other hand, virulent hemolytic streptococci have been found in preponderating numbers in the noses and throats in these cases of influenza which suggest strongly that these streptococci play an important rôle in the etiology of these epidemic infections. The conclusion is certainly warranted that the influenza bacillus was of no primary importance in the causation of this epidemic of "grippal" diseases.

In regard to the epidemic of acute respiratory diseases in horses that occurred simultaneously with the human epidemic during the winter of 1915-1916, the accumulated evidence strongly suggests that the causative factor was also a hemolytic streptococcus. This streptococcus derived from equine sources, although similar in many cultural and morphologic characteristics to the streptococcus from human sources, differed from the latter in its biologic reactions, a fact which renders improbable a common etiology for the 2 infections. The pathogenic properties of each type of streptococcus for each specific host were quite similar. Furthermore, it is interesting to note that the conditions under which the 2 outbreaks of respiratory diseases occurred in man and in horses were quite analogous from the epidemiologic point of view. The activity of the horse market during the past year, the collection of large numbers of horses from the agricultural districts of the United States into concentration yards, and congested shipping facilities occasioned by the abnormal demand for horses created an artificial environment which simulated quite closely the crowded state of living among human beings — a factor apparently highly important in the transmission of these epidemic respiratory diseases. The disease prevalent at first only in the large concentration markets, rapidly spread along lines of transportation until horses in the more remote parts of the country were attacked.

This study of 2 diseases, apparently caused by 2 organisms of similar morphology and cultural characteristics, but differing in their pathogenicity for other hosts, occurring under similar epidemiologic conditions and characterized by identical pathologic lesions, emphasizes the importance of comparative pathology in the development of human medicine.

DISCUSSION

D. J. DAVIS: It seems remarkable that Pfeiffer's work on the cause of influenza has attained so much prominence in medical literature. It is true that at that time, 1892, and shortly after, his observations, as far as they went, were supported by a number of investigators, especially German, but in analyzing the data one notes that his work has little connection with the influenza pandemic of 1889-1890. He isolated and cultivated the influenza bacillus 2 years after the great epidemic, during the appearance of a smaller and more local epidemic of 'grippe.' In his paper he states that he remembered seeing the small bacilli in sputum preparations from cases of the epidemic 2 years before and he had preserved some of the slides and also photographs of the smear preparations. This was the only connection existing between his work and the pandemic. It is interesting to note that others had isolated cocci, especially streptococci and pneumococci, in practically all cases examined in the great epidemic and considered them the cause. Pfeiffer at that time did not know that influenza bacilli could be found in nearly all cases of whooping cough and commonly in cases of measles, bronchitis, chickenpox, scarlet fever, etc. His control observations were not extensive. His contribution seems to be good bacteriologic work but not convincing in establishing a causal connection between an organism and a disease.

The entire group of the 'influenzal' infections is in many respects comparable to the group of conditions that we designate 'rheumatism,' and just as we are analyzing rheumatism into a number of separate diseases so we are beginning to cut out, as it were, from the heterogeneous group of influenzas, certain pretty well defined diseases. For example, streptococcus sore throat, a condition often passing as a 'cold,' is a definite infection, in every way as definite as measles or scarlet fever. So in the lower animals are diseases like the one which Dr. Mathers describes in horses, definite both clinically and etiologically. In rabbits is the interesting respiratory disease of rabbit influenza or snuffles, occurring in epidemic form and caused by a small bacillus somewhat similar to but in many ways different from the influenza bacillus. This is likewise a definite clinical and pathologic entity. Careful study is therefore disintegrating the large heterogeneous clinical groups of symptoms in both man and animals into well defined diseases with distinct etiology.

A. I. KENDALL: Dr. Mathers presents the subject in an interesting and instructive manner. First, his observations would indicate that the old idea of a definite clinical syndrome associated with a definite and specific organism was not entirely justifiable. In the 2nd place, we have a disease in man and a coincident epizootic, similar to its pathology and causation, in the horse.

With reference to the 1st feature, the relation between a rather definite syndrome in these cases, of the influenzal type, and a definite organism not the influenza bacillus, it appears that the old conception of its etiology must be given up. There are many instances where diseases once thought to be due to a single organism are known to be excited by a variety of organisms; this is equally true of pathologic lesions. Thus, we have in the diphtheric membrane as it occurs in the throat the disease diphtheria, and we recognize a diphtheritic membrane in the intestinal tract as well.

Of greater importance to public health, however, is the association of organisms, very similar but exhibiting slight differences, perhaps, with diseases that occur simultaneously in man and in animals. We have in bubonic plague, of course, a similar and better known example of such a coincidence, from

which, furthermore, we may infer a mechanism of the reservoir in nature of pathogenic organisms from which in time they may return again to infect man. In the case of bubonic plague we know there is such a reservoir for the organism and we know furthermore that from time to time the disease spreads from the reservoir (rodents) to man, and that the organism exists in these rodents before every new outbreak.

We have to consider finally the carrier possibility, and that the slight differences found by Dr. Mathers in these streptococci may be analogous to differences in the plague bacillus. It is a striking fact, borne out by epidemiology, that the plague bacillus infection which produces buboes rarely appears in the pneumonic form. Thus the bubonic form of plague will usually develop from the bubonic type, and the pneumonic from the pneumonic type.

It may be that streptococci found in man and in animals may likewise exhibit the same or similar manifestations. At present the question of immunity is not definitely settled. It is conceivable that future investigation will demonstrate the existence of a group of streptococci that may play a part in these infections, but this is not certain.

We have no assurance that the methods by which we now judge streptococci are those which ultimately will prevail. Thus, there are morphologic and, to a limited degree, cultural characteristics utilized at present to effect differentiation, but these and even some of the pathologic properties of the group, are not necessarily the ones that will finally be utilized for this purpose. The streptococcus appears to be protean in its manifestations, and final judgment concerning it must be withheld for the present.

Frank Billings: I should like to ask Dr. Mathers to make a statement relative to the use of autogenous antigen in the horse. What effect it had immunologically and therapeutically?

George Mathers: In reference to Dr. Billings' question, we have used streptococcus antigen prepared in the ordinary way; it represents nothing more than a killed suspension of the equine streptococci. We have used it more as a prophylactic measure than a curative measure. As a curative measure, we have not seen anything that would indicate it is of any great value. As a prophylactic measure, so far as we can determine, it seems to have some beneficial effect; that is, horses that are injected about 10 days or 2 weeks before they are shipped into the uninfected market seem to resist infection better than the horses in the agricultural districts which are shipped into the market without vaccination. With our present knowledge, it is impossible to make any definite statement at this time. Experiments of a more definite character are going to be put into effect this winter.

In making cultures of pneumonia sputum, using the intraperitoneal method, which is the injection of a suspension of the sputum and removing cultures in 18-24 hours from the peritoneal cavity in the mouse, it is not uncommon in such cultures to find the influenza bacilli from the sputum of cases of frank lobar pneumonia. When using blood agar plates in culture work the influenza bacillus appears to be often present in all kinds of infections of the respiratory tract.

THE TREATMENT OF GONOCOCCAL INFECTIONS BY THE INTRAVENOUS INJECTION OF HOMOLOGOUS AND FOREIGN PROTEIN

Harry Culver

November 7, 1916

After the intravenous administration of a highly polyvalent gonococcal vaccine, Bruck and Semmer in 1912 and 1913, observed striking therapeutic results in gonorrheal complications, especially arthritis, epididymitis, and acute prostatitis. These results, within certain limits, ran parallel to the severity of the reaction following each injection. A specific temperature increase was noted, which was higher in gonorrheal than in nongonorrheal patients; hence this method was suggested as a diagnostic as well as a therapeutic agent. At this time the entire process was attributed to the production of specific immune substances, by the intravenous injection of gonococcal vaccine.

It has been clearly demonstrated that in typhoid infections, a nonspecific reaction follows the intravenous injection of colon bacilli, pyocyaneus bacilli, and secondary proteose preparations. These substances give results clinically and therapeutically quite like an injection of killed typhoid bacilli.

In order to determine the degree of specificity, if any was present, following the intravenous injection of gonococcal vaccine, 4 series of patients suffering from gonorrhea and some complication, such as arthritis, epididymitis, or acute prostatitis, were chosen in the order in which they had entered the hospital, no attempt having been made to classify them as to severity or complication. The 1st series was treated intravenously with a strongly reacting dose of gonococcal vaccine; the 2nd series received a similar dose of meningococci; the 3rd series received a suitable dose of colon bacillus vaccine; and a 4th series was given a deutero-albumose solution.

When possible the patients were kept in bed throughout the treatment, special care being taken to keep them quiet for 2 days following each injection. No local or internal treatment was given for the gonorrheal infection other than mechanical support. The temperature, leukocyte, and differential counts were made just before each injection and at regular hours thereafter for the first 48 hours.

Gonococcus Vaccine. — The 1st series of 13 patients was given intravenously one hundred million killed gonococci, and the same or slightly varied dose repeated every 4th or 5th day. The greatest number of injections given 1 person was 6, most of them received 5, while 1 received but 1 injection.

The injections were followed by a chill of variable severity coming on in 20 minutes-1 hour and lasting 15-30 minutes. This chill may or may not be accompanied by headache, which is usually of short duration and passes away shortly after the chill is over. Exceptionally, there is nausea and vomiting during the first few hours, but it is never severe and always transient. This occurs more often in patients who have disobeyed instructions by eating heartily within a few hours of the injection.

At the onset and during the chill the patient often complains of severe pain in the affected parts. Whether this is due to some internal cause, or to the unavoidable motion produced by the chill, it is impossible to say. However, the pain is variable in different patients and in the same patient at different times.

Invariably the disagreeable effects of the reactions, if any have appeared, disappear in about 24 hours, and for the next 24-72 hours a variable degree of comfort is experienced. The pain and the tenderness together with the swelling of the joints is much improved. However, this prompt improvement is most likely to be of only 2-4 days' duration, and then there is a stiffness of the affected joints with some pain on motion, but usually in a much less severe form.

These relapses gradually decrease in severity following successive injections until eventually none appear. In some instances there may be none, even following the 1st injection.

Jobling and Petersen have found that there is a marked mobilization of serum protease following the intravenous injection of bacteria. Serum protease is believed not to act on bacteria as such, but may act on toxic protein-split products of bacterial origin which previously existed in the blood and tissues, breaking them down to lower and nontoxic substances. This process of detoxication would account for the well-being of the patient for the 24-72 hours following the injection; however, the infectious focus may still be present to reproduce a similar condition of intoxication later, as actually does occur at times on the 3rd-5th day following an injection.

The gradually decreasing severity of these relapses could also be explained by an equally gradual destruction of the infectious focus by other factors entering into the reaction to be mentioned.

Injections are, therefore, repeated on the 3rd-5th day, or usually just as the joints begin to show a return to their old condition. This seems to be a more efficient method of injecting than the daily injections. With daily injections, the patient is at all times having a reaction or just recovering from one. His general condition is not so good nor does the local disease respond so well.

It is usual for the severity of the reaction to decrease following repeated injections, and this decrease is directly proportional to the number of injections previously given. In order to maintain a constant reaction with each succeeding injection, the dose should be gradually and cautiously increased.

In 2 of these patients, both of whom had numerous subcutaneous injections of gonococcal vaccine, there appeared immediately following each intravenous injection a very transient reaction characterized by flushing of the face, cyanosis, dyspnea, and a tingling sensation over the surface of the whole body. These reactions lasted 1-2 minutes, after which the patients felt perfectly at ease until the usual reaction appeared in 20 minutes-1 hour. This anaphylactic-like reaction may have been due to a partial sensitization from the previous subcutaneous injections. Three other patients in this series developed a mild type of a very similar condition, on the 3rd intravenous injection.

The typical temperature curve following these injections revealed a slight fall during the first part of the chill, followed by a gradual rise, which reached its maximum in 4-6 hours, and gradually fell to normal in 24 hours.

The leukocyte counts during a reaction and following it are somewhat variable. Usually there is a mild leukocytosis just before and during the first part of the chill, soon followed by a marked leukopenia, which appears toward the end of the chill; a count as low as 2000 has been observed repeatedly during this stage of the reaction. This condition is soon followed by a gradually developing leukocytosis which reaches its maximum in 5-7 hours, and remains moderately high for 24-30 hours. A return to normal occurs in about 48 hours.

This marked and sudden change in the leukocyte count is due almost entirely to an increase or decrease of the polymorphonuclear leukocytes in the peripheral circulation, their percentage having as low

as 50 during the leukopenia stage, and as high as 96 during the height of leukocytosis.

Meningococcus Vaccine.—The 2nd series of 15 patients was treated with killed meningococci in the same dose and at similar intervals as in the gonococcus series.

The reactions as far as could be determined were similar in every detail to those produced by the gonococcus vaccine. One instance of a double reaction occurred following the 1st injection, and 1 patient developed this condition after 2 injections. None of this series had had previous subcutaneous or intravenous injections.

The leukocyte curve, in general, likewise followed those of the 1st series very closely. The type of cell varied as in the 1st series. One very startling difference was observed between the 2 groups. Over one half the meningococcus series developed a more or less severe herpes of the lips and mucous membrane of the mouth, first appearing in 48 hours and remaining for 4-7 days. This condition did not follow any but the 1st injection, and did not become aggravated or recur when further injections were made in a susceptible person.

Colon Bacillus Vaccine.—This series contained but 9 patients. The reactions were in every way like those produced by meningococcus and gonococcus, with the exception that the size of the dose required to produce the same results was very much less. At first a dose of 100 million organisms was given, but the reactions were so severe that 25 million were finally used as the initial dose, this to be increased if necessary to produce the desired results.

Deutero-Albumose.—A secondary proteose made from casein was used (80 mg.) in 4% solution on a series of 4 patients, the initial dose being 2 c.c. The reaction showed some variations from those produced by bacterial suspensions, in that the chill never took place before 1 hour after the injection, and that there was no headache or nausea following any of the injections; also the fever and leukocytosis did not reach the height produced by bacterial suspensions. This is, no doubt, in part a matter of dosage. Sufficient experience with this solution, however, has been had to convince one that the reaction and therapeutic effects are very similar and equally as effective as those produced by bacterial suspensions, as well as giving rise to less disagreeable reactions.

There seems to be no question that the curves representing the reactions produced following the injections of each organism and albumose are very similar; however, the curves representing the colon

bacillus seem to reach a higher point in both instances; this is due to the smaller number of injections represented in the curve. The crest of a curve of this kind is obviously not as high as one representing a single individual reaction, since the time of maximum temperature and leukocytosis may vary somewhat for different persons or for the same person at different times.

As far as therapeutic results are concerned there is no noticeable difference between the 3 bacterial suspensions or the albumose solution. To produce results therapeutically a reaction is necessary. That is, a chill must occur which is invariably followed by the temperature and leukocyte changes noted. A dose insufficient to produce a definite chill is not followed by as marked a temperature and leukocytic reaction, and clinically not only is there no therapeutic benefit derived, but also the patients become more uncomfortable than before. The reactions following injections in nongonorrheal patients are not to be distinguished from those produced in infected patients.

These observations were made by injecting a series of patients with chronic skin lesions with no history or indication of gonococcal infection. The size of the dose required to produce a reaction, the chill, temperature, and leukocytosis were alike in every way in the infected and the noninfected patients.

Thirty-one patients suffering from arthritis associated with gonorrheal urethritis were treated. Most of these cases were acute or subacute, but some were of 5 months' duration, and many were over 10 weeks' duration when the treatment was begun.

As might be expected, the most striking results were obtained in the acute and subacute cases; however, the most refractory instances were also in the acute class. Those suffering for long periods appeared to respond more slowly to the treatment, but fortunately seemed to suffer from no recurrence or new joint involvements during the course of the treatment. All but 3 of the arthritic patients were apparently completely cured or manifested a decided improvement. The length of treatment varied from 2 days to 1 month.

Unusual effects were seen in 3 patients with acute arthritis, so severe that sedatives were necessary to give them rest for the first 2 days in the hospital. After a single reacting dose in each instance they felt so well that they insisted on getting out of bed, and in 3 days they walked from the hospital. Two of the patients had effusions in the knee joints, which completely disappeared before their discharge from the hospital. Unfortunately, none of these men has been heard

from since, so the permanency of the striking results in these instances is not known. Equally striking was the instance of a man who had been confined to his bed for 4 weeks with arthritis of almost every joint of both lower extremities. These lesions had come on during the 3rd week of gonorrhea. After the 3rd injection, he was up and walking about, and after the 6th injection he was apparently completely cured. He went back to his work as a cook and has been at work for 5 months with not the slightest indication of recurrence.

The 3 refractory cases mentioned were all acute, and seemed not to respond at all or very slowly to this form of treatment. One would show considerable improvement for a day or 2, but invariably would lapse back to the original condition; a 2nd recovered completely excepting one knee joint, which contained a marked effusion and seemed not to be affected by repeated injections, while the 3rd did not respond from the first to repeated injections of albumose solution.

Bruck noticed similar refractory cases which he explained by the absence of the homologous gonococcus strain from his polyvalent vaccine. It is now evident that this explanation will not suffice, but whether it is due to a special resisting power of the particular infecting gonococcus or to some peculiarity of the infected host, it is impossible to say. Such patients react with fever and leukocytosis as do all others.

Twelve patients with acute epididymitis were treated, and invariably the pain would subside after the 1st injection. Usually not more than 2 injections were necessary, and indeed in most instances 1 to effect a cure. The swelling began to subside within 24 hours after the 1st injection. In no instance did the patient remain in the hospital over a week, excepting in 1 case in which an overdose was given.

That these injections are not prophylactic against the development of new complications is evidenced by the fact that occasionally one sees a patient under treatment, develop an acute epididymitis or an involvement of a new joint. Again, a patient may leave apparently cured of arthritis to return in a few weeks suffering from epididymitis.

An attempt was made to follow these patients after their discharge from the hospital. Five months have now elapsed since the 1st were discharged, and with 3 exceptions, all have been away for at least 3 months. Other than the development of acute epididymitis in 3 patients after their discharge, there have been no complications or recurrences of any kind.

On account of the fact that the reaction following these injections is followed by a chill and general reaction of more or less severity, a very complete physical examination is necessary beforehand. Such a reaction necessarily calls for increased cardiac activity, so one should proceed with caution when a patient with a coexisting organic heart disease presents himself. The smallest reacting dose of meningococci was given to one man who was suffering from mitral regurgitation of long standing but perfectly compensated, together with acute epididymitis. He passed through the chill with no distress, but in 3 hours after the injection he became cyanotic, his pulse became irregular and feeble, and he had marked precordial pain. This condition lasted 10-15 minutes, and he had no further inconvenience. No other cardiac irregularities were noted in the entire series. Arnold and Holzel cite Lewinski's case of acute cardiac insufficiency developing after the intravenous injection of gonococci. Heart disease was not known to be present. On the other hand, Luithlen reports a case of gonorrheal endocarditis successfully treated in this manner. There are many instances reported, however, of cardiac symptoms developing in the presence of organic heart disease following these injections, so one should exercise care and judgment in the selection of cases.

From the proper dosage in this series, there were noted no other symptoms attributable to the injections. Special attention was given the kidney function, particularly in 3 patients who had received large doses of colon bacilli. In no instance did albumen appear in the urine, or did any indication of kidney involvement arise. One patient having a chronic diffuse nephritis with considerable albumen in the urine had 2 injections with no appreciable change in the kidney function.

This seems to be significant, as Breed and others had found that there is quite a marked increase in nitrogen output after such a reaction, this increase being maximum on the 6th day. She advises a low protein diet for a few days before such injections to prevent a possible kidney change.

Chiray has found that foreign protein injected intravenously soon disappears from the circulation, taking with it an appreciable amount of protein from the blood. He frequently produced albuminuria in man in this way, especially in patients who already showed renal insufficiency. Marked structural changes were found in rabbits by repeated injections. The material injected or the intervals of injection were not given.

Foekler reported epileptiform seizures after similar intravenous injections, and Fischer in 1 instance noted cerebral symptoms, which passed off in 24 hours.

Delirium was noted in 3 patients of this series, all of which had received large doses of colon bacilli.

COMMENT

It is apparent that any therapeutic effect obtained by the intravenous injection of killed bacteria or albumose solution is not due to any specific reaction, in the sense that antibody-production is stimulated by specific substances contained in the organisms; however, Dunklin using proteose-injection in typhoid-immune rabbits found a decided increase in the antibody titer, for typhoid bacilli, which is explained by a selective stimulation of the hematopoietic system by a nonspecific substance. Walther, Hildebrand, Englehardt, Rolly, and Meltzer have reached the conclusion that high temperature artificially produced has a favorable influence on any established infection; on the other hand, cold seems to retard the formation of immune bodies. The optimum temperature for the growth of the gonococcus in vitro is 97-98 F. Any appreciable increase in temperature has a very deleterious effect on the life and growth of the organism. A sudden rise to 102 F., or over, means certain death of the culture.

When acute epididymitis develops and recovers, does the fever produced thereby have anything to do with the spontaneous cure of gonorrhea? Many patients with infections terminating thus have had considerable fever during the onset of the complication. On the other hand, patients are seen with infections terminating in a similar manner having had a normal temperature throughout; this, however, does not seem to be a common occurrence.

Experimental urethritis in man has been produced, but Finger, Ghon, and Schlagenhaufer[1] regularly failed when the experimental patient had a temperature of 102.2-104 F. due to some preexisting disease.

A patient recently entered the hospital with acute urethritis of 3 days' duration. A positive gonococcus culture was obtained on entrance. The 2nd day in the hospital he had a chill, followed by a temperature of 105 F. Malarial parasites were found in the blood, but the chills and fever were allowed to continue for 4 days, at the

[1] Cited by Kyaw: Med. Klin., 1912, 8, 1829.

end of which time all evidence of local infection had disappeared. He remained in the hospital for 2 weeks, without recurrence of the infection, having had no local treatment whatever. Equally noticeable is the influence of fever on these infections in the medical wards; one rarely, if ever, sees a gonorrheal infection coexisting with some fever-producing disease like pneumonia, typhoid, or malarial, while gonorrheal infections are relatively common among the chronic nonfebrile conditions.

By the intragluteal injection of boiled milk or sodium nucleinate, Muller and Weiss[2] produced temperatures as high as 104.7 F. in 6-7 hours. Very satisfactory results were obtained in epididymitis, prostatitis, and arthritis by repeated injections. Smith,[3] using normal horse serum had results corresponding favorably with those produced by antigonococcic serum in gonorrheal complications. His therapeutic results ran parallel to the reaction produced, which in turn was proportional to the temperature obtained.

On the other hand, Jobling and Petersen claim that intravenous injections cause a fluctuation in the ferment-antiferment balance of the serum as well as changes in the coagulation mechanism and the opsonic and complement properties. "No single factor seems to be responsible for all of the changes resulting from this fluctuation, but a whole series of events is started all of which tend toward a condition favorable for recovery from infection." That there are factors at work other than fever seems probable. Miller and Lusk have found striking therapeutic results in arthritis due to other infections than gonorrheal, as well as in gonorrheal patients, by the intravenous injection of typhoid vaccine. These results, obtained in patients with nongonorrheal arthritis, could not be consistently attributed to fever alone, as the streptococcus and other organisms commonly associated with this condition are known not to be especially heat sensitive. Again, why should a sionally still harbor like cultivable gonococci? The temperature and patient completely recover from arthritis by this treatment and occa-leukocytes presumably being equally distributed, why should the organisms in a joint disappear and those in the urethra remain? Numbers and arrangements in clumps may be of some importance while a less resistant organism may be developed by its growth on a new type of tissue.

[2] Wien. klin. Wchnschr., 1916, 29, 249.
[3] Jour. Am. Med. Assn., 1916, 66, p. 1753

The therapeutic results in the group which forms the basis of this report very noticeably correspond to the temperature increase and to hyperleukocytosis. Considering the facts that the gonococcus is heat sensitive both in vitro and in vivo; that fever patients cannot be experimentally infected with the gonococcus; that a fever-producing disease spontaneously cures previously existing gonorrheal infections, there can be but little question that fever artificially produced plays some part in the recovery from these infections.

How much influence, if any, the leukocyte increase in the peripheral circulation has, cannot easily be determined, for when artificially produced in the manner employed here, the fever and hyperleukocytosis are invariably present together.

It is apparent that the usual treatment of gonorrheal arthritis is not satisfactory in all instances, when almost daily one can see an ankylosed joint and atrophied muscles following this condition. Should this treatment by intravenous protein injections prove to give permanent results in these conditions, as present data seems to indicate, are we justified in using such measure? In view of the chronicity of the disease and the destructive complications that commonly arise it would appear to be a rational procedure when properly used and controlled. However, until some substance is obtained whose dosage can be more definitely standardized, it would seem that this form of treatment should not be generally used by those not thoroughly familiar with the reaction and the manner of regulating the size and interval of dosage of such, as used in the work here reported.

DISCUSSION

ERNEST E. IRONS: The part which nonspecific reactions play in the production of the phenomena of infectious diseases is a subject of live interest, and in the study of these reactions a number of questions arise, some of which are startling to the orthodox adherent of the theory of complete specificity in biologic reactions.

Before considering some of the questions which are suggested by the interesting reactions described by Dr. Culver, it it desirable to point out how great a departure from the hitherto accepted views of immunity, this discussion entails.

Specificity in biologic reactions has been the guiding principle of those who have attempted to devise methods of therapy in infectious diseases. The theory of antigen and antibody, developed by the genius of Ehrlich, has dominated therapeutic research. His conceptions of strict specificity in the relation of the reaction products of the animal body to foreign protein, whether bacterial or other in origin, have been repeatedly questioned, but while his theories have been modified to meet the requirements of physiochemical principles, the fact remains that it has been under their guidance that our most valuable specific remedies, such as antiserums for diphtheria, tetanus, and meningitis, salvarsan,

prophylactic immunization against typhoid, and diagnostic aids, based on agglutinins, precipitins, and complement-fixing substances have been developed.

In entering on a consideration of the possible nonspecific elements in the phenomena of disease, it is not proposed therefore to supplant the older specific conception, but to discover in what ways these nonspecific reactions help or hinder the specific factors, or act independently of them.

It is also important to bear in mind that the specific biologic reactions which present so high a grade of specificness that we have come to regard them as something apart from ordinary chemical reactions, are after all merely instances of physicochemical processes, whose fine degree of adjustment can be attained only under conditions met with in the animal body. The phenomena of agglutination, phagocytosis, and precipitation can all be produced artificially, though less perfectly than by using materials from the animal body, by properly adjusting the concentration of electrolytes, or by modifying the surface tension of nonmiscible fluids, etc.

And so no matter what the ultimate conclusion as to the nature of the nonspecific reactions may be, it is altogether probable that they follow the same chemicophysical laws as do reactions which we have come to regard as highly specific.

The first question we may ask is: In the course of and recovery from infectious disease, to what degree are specific and nonspecific factors concerned?

To refer to concrete examples:

Natural immunity to the gonococcus is the rule in animals, and, on the other hand, is practically never seen in man. Suitable bacterial food supply, vigor of growth, oxygen tension, temperature, moisture, and the absence of hostile substances and cells are among the conditions which make invasion of the host possible. Even in man, who is usually nonimmune, some of these conditions vary with age and physical condition of the host.

That specific immunity to the gonococcus is acquired by the human subject of infection is shown clinically by the usual recovery from infection, even though it be extensive, and immunologically by the appearance of specific immune properties in the blood, as demonstrated by reactions of agglutination and complement fixation. The immunity of gonococcal infection is subject to relatively rapid fluctuations, demonstrable both clinically and by laboratory methods, and in this respect differs from the relatively more permanent immunity of typhoid infection. It may also be modified by the injection of gonococcal protein as demonstrated by studies of complement fixation.

Of the nonspecific factors, fever has long been known to influence the course of infection, although accessions of fever alone are not sufficient regularly to destroy the gonococcus, for it may be recovered from the blood and joints in patients who for days have suffered from high septic temperatures.

Leukocytosis, the absence of which in typhoid has been emphasized as a factor possibly retarding recovery, is usually present in gonococcal infections, even in those rapidly progressive.

In typhoid fever the specific factors, so far as we know them, seem to be opsonins, lysins, and, from recent studies, also the agglutinins.

Of the nonspecific factors in the production of the symptomatology of typhoid, we note that Vaughan years ago suggested that the fever of typhoid was caused by products of splitting of typhoid protein, and he was able to produce various types of fever in animals by the injection of protein-split products obtained by hydrolyzing bacterial protein of colon or other bacteria, or egg white.

Phagocytosis both endothelial and leukocytic seems to be important. Polynuclear phagocytosis is facilitated by specific opsonins, and Gay maintained that the hyperleukocytosis following intravenous injections of typhoid bacilli was also specific in that it was more pronounced in animals previously immunized than in nonimmunized animals. Other investigators have failed to confirm Gay's work in this respect, and find that the hyperleukocytosis is nonspecific, and may be elicited as well in untreated as in treated animals.

When pulmonary embolism occurs in typhoid fever, the symptoms are very similar to those seen after intravenous injections of foreign protein. The crisis in pneumonia also is similar in many ways to the reaction described. Nor are the phenomena of the reaction peculiar to patients suffering from febrile disease, for McBride and Kibler have observed the same reaction in a normal man injected intravenously with typhoid vaccine.

Several theories have been advanced to explain the change in the clinical picture and disappearance of previous symptoms of disease following intravenous injections.

Jobling and Petersen have shown that the serum protease of the blood is increased by intravenous injection of protein, and suggest that the ferment normally held in check by antiferment is freed by the removal of the latter, and at once acts on the toxic fever-producing substances in the body, breaking them down to nontoxic elements.

This conception receives support from the older experiments of Bordet.

Friedberger found that when bacteria were mixed with fresh serum, and later removed, that the serum became highly toxic, and he called the toxic substance supposedly derived from the bacteria anaphylatoxin. But following the lines suggested by the work of Bordet, other workers found that by mixing serum with kaolin, they could produce equally as toxic a product, and have argued that the toxic substance, whatever it might be, was derived in both instances from the serum and not from the bacteria.

It has been suggested, also, that the ferment action of serum in the Abderhalden reaction is directed against protein elements of the serum itself and not against the protein of the substrate.

The hyperleukocytosis which accompanies the reaction has also been held to accelerate the phagocytic removal of invading bacteria. This seems in part a nonspecific factor.

It is also a question as to how far the reaction produces indirectly a specific effect by mobilizing or calling in action specific immune substances which have already been formed but have not developed their maximum action in the body of the patient.

Perhaps the most important question of all is: To what extent may these nonspecific methods be at present employed in therapeusis with profit and at the same time safety to the patient?

It must be evident that our knowledge of what takes place in the body of the patient is largely theoretical.

The striking results, often apparently beneficial to the patient as outlined by Dr. Culver, are sufficient to demand further consideration. The 40% of critical drops in temperature and permanent defervescence obtained by Gay in typhoid cannot be put aside, although one feels impelled to emphasize, perhaps more than he, the obviously nonspecific character of most of the phenomena including hyperleukocytosis.

But in spite of the sometimes brilliant clinical improvement we cannot overlook the severe reactions, the instances of cardiac dilatation, and also the

occasional, though rare, deaths which have at least followed, if they have not been due to the injections.

It is possible that methods may be found of obtaining the favorable non-specific effects without exposing the patient to the rigorous experiences of present methods, but this is an end not yet achieved.

The need for special caution is perhaps less imperative in treating gonococcal arthritis than typhoid or pneumonia. In pneumonia, Mathers concluded from his observations that he was not justified in continuing this method of treatment.

There seems to be no question but that certain patients suffering from non-gonococcal infectious arthritis undergo a rapid though perhaps temporary improvement. I have had occasion to observe a number of cases of infectious arthritis so treated by others. Some of these who improved following the injections later returned as badly crippled as before. After we had removed the infectious cause of the arthritis, they again improved, and this time did not return. There is always the danger that routine use of a nonspecific and empiric remedy may lead to incomplete study of patients.

It is also worth noting that the enthusiast for intravenous injections would hardly maintain that the most successful reaction can ever restore function of destroyed joints.

The study of the nonspecific elements in disease is of great importance, perhaps greater than we now realize, and promises to open for us new avenues of attack, and viewed from this angle, this subject deserves a full and free discussion.

From a therapeutic point of view, however, I believe we may well join with Dr. Culver in warning against the indiscriminate and general use of these methods, until they have been more thoroughly studied. The balance of immunity is a very delicate one which may easily be deflected for or against the patient, and we shall not wish to alter this balance unless we can be sure that the change will be under our control and uniformly in favor of the patient.

William Petersen: Dr. Jobling and I took up work along this line 2 years ago following a study of the crisis in pneumonia. It is quite evident that the explanation which has been given us for this phenomenon, the antibody theory, does not cover the situation completely. The changes which are found in the concentration of the antibodies are hardly sufficient to account for the rapid and complete clinical change which occurs during the crisis. In the study of a series of cases of pneumonia we found certain serum changes which were quite uniform in all cases, that is, mobilization of the nonspecific protease and erepsin at the same time that a diminution of antiferment was noted. At the time that we were making these studies, Lüdke reported the first use of proteose in typhoid fever. We have studied approximately 35 cases of typhoid, and have given most attention to an effort to find out the mechanism and the changes which occur in the serum and in the body rather than the clinical effect in typhoid fever. Great caution should be used in this form of treatment, not because the proteoses and vaccines which are used are in themselves so toxic, but because of the profound intoxication which may occur when many bacteria are rapidly destroyed in the body. We have used a preparation of proteose of which one may give half a gram to a dog without toxic effect, yet we have seen effects from 10 mg. in typhoid fever, which were decidedly alarming. In that series of 35 cases there were 4 deaths. One occurred 24 hours after injection in about the 4th week, and quite toxic before injection. We had one other case in an obese woman, early in the disease,

who died within an hour after the injection, with toxic manifestations. Necropsy showed an acute myocarditis, and certain fatty changes. We have had two other deaths in early cases; they were selected with great care, yet both patients had intestinal hemorrhages, and died within 24 hours.

Immune bodies are mobilized after injection of proteoses, which might have a marked influence, according to the work of Bull. We may expect an agglutinin reaction to be of considerable importance, and phagocytosis would account for some of the reactions.

Inasmuch as all these injections are made intravenously, and serum plays so marked a part in it, it is more than probable that the physical condition of the serum is of some importance. This is indicated by the fact that all the substances injected into the blood, colloidal metals, ferments, vaccines, distilled water, salt solution, etc., all produce the same result clinically, and probably act in one and the same way in bringing about the result.

Undoubtedly the reaction has a certain therapeutic benefit. I am not prepared to state the exact value of it, but we feel that it deserves emphasis in so far that certain definite changes do occur in the blood and cells, undoubtedly nonspecific but which must be considered with the specific reactions which have been studied and known for a considerable time.

Frank Billings: As to the statement by Dr. Culver that a fever of over 102 F. is likely to result in the death of the gonococcus invading the tissues, that may be so in local infection, but it is not true in gonococcemia, especially when associated with ulcerative endocarditis. One often sees a patient living sometimes for days and weeks with a septic temperature running to hyperpyrexia. The gonococcus now seems to become modified, to take on new qualities which protect it against the host. The gonococcus may remain alive in the circulation in spite of the high temperature under those conditions.

In my experience, which has been rather large in cases of arthritis, and in gonorrheal infections, as well as in what we call streptococcus infection of the joints, we have used only in a very few instances intravenous injections of protein. I should like to ask, in speaking of chronic joint infections and of recovery, if it is meant that in chronic cases the tissue changes are removed. In most of my cases, while we may remove infection and stop the further progress of the disease, there are some tissue changes from which the patient will probably not entirely recover.

I doubt if I shall use vaccines any more in treatment, certainly not in chronic joint infections of any kind, or in gonococcus infections. If one can find the focus of the infection, removal of that usually is followed by prompt recovery of the joint infection in chronic cases. With proper hygiene, after the removal of the source of the infection, these patients may make good recoveries without any intravenous or other injections.

Joseph L. Miller: Recently autoserums have been used in various skin lesions and so on. Goodman reports the sudden termination of chorea after the intraspinous injection of the patient's serum. He took blood from the patient, separated the serum, injected it, and the chorea terminated by crisis. This form of treatment may be regarded as analogous to the use of foreign proteins.

At the present time we have used foreign protein in 115 cases of arthritis; 45 of the last 85 cases were cases of acute arthritis, and in 29 of these the disease terminated in 1-4 or 5 days. In 23 the results were permanent. Six had a relapse. I have noticed, as Dr. Culver reports, that the results in acute gonorrheal arthritis are not as satisfactory as in the chronic form. I observed also

that in gonorrheal arthritis there was less likelihood of a relapse than in the cases of ordinary streptococcus arthritis. The results in some of these cases are most striking: A patient with a high temperature and arthritis, after a single injection of typhoid vaccine, within a few hours not only improves but has a crisis and is cured, the joint symptoms all disappearing. In some cases, after a single injection, the disappearance of symptoms is permanent. In other cases several injections are necessary to prevent relapse. But the striking result that can be brought about in a few hours, in a patient with very acute arithritis, is something of great interest.

In the cases I have treated during the last 6 or 7 months, a large number had received without benefit large doses of salicylate of soda, and they reacted well to foreign protein also.

In the 115 cases there have been no deaths. On 2 or 3 occasions most alarming symptoms have developed. I have not given vaccine to a patient who had what we thought was a bad heart, but nevertheless we have had in 2 or 3 cases alarming symptoms: the patients have become almost pulseless after moderate injections.

A year ago I treated typhoid cases with proteose or typhoid vaccine, and it is most interesting to see how one may at times terminate typhoid fever within a few hours; but neverthless, after watching the reactions last year and this year, I am not using typhoid vaccines in many cases, because it would be a calamity to have a patient die after such an injection—for instance, from hemorrhage. So I have some timidity about repeating typhoid vaccine this year, although last year it gave favorable results. Whether we shall continue to use this method in arthritis time will tell. I feel that it ought to be used with great care. and only in patients who have been carefully selected so far as their cardiac condition is concerned. Whether there will be proof furnished of any difference in the effects of these foreign proteins, time will also tell. We have a patient now with gonorrheal arthritis of 2 years' duration, who received typhoid vaccine without any results. A few days ago the patient had 2 injections of gonococcus vaccine with striking results. Apparently, in that particular case, we obtained no results with nonsensitized typhoid vaccine, but we did with gonococcus vaccine.

H. CULVER: The patients I had were suffering from relatively acute conditions, of 5, 6, or 7 months' duration, at the most, and no definite organic change in the bone, overgrowth, or destruction had occurred.

It is a fact that the gonococcus is heat sensitive; it is also easily acclimated to new surroundings. The gonococcidal power of rabbit serum for ordinary gonococci may be 1 to 75, but by continual transplantation in rabbit serum, such strains become resistant so that they may grow in rabbit serum 1:4.

Similarly, by gradually increasing the temperature at which the organism is cultivated, it eventually may grow in a temperature which, if thrust on it suddenly would cause its death. It may grow in a temperature of 102 F. if gradually accustomed to it.

SUCCESS IN THE TREATMENT OF CANCER

EMIL RIES

December 5, 1916

It helps once in a while to go over our daily work and find out how sound the foundations of our much vaunted progress are. If I were to tell you the great advances which have been made in the treatment of cancer in the last year, I might as well sit down. There have been none. Since the knife has been used no advance has been made except the more extensive use of the knife.

Perhaps we would feel better about this if we had learned more about the pathology of carcinoma, if we had learned what it is, what causes it, what is the starting point. As it is, all the experiments that have been carried out in animals and human beings have so far been useless. The experiments in animals do not deal with the identical thing which we have in human carcinoma. No one has ever transplanted carcinoma from the human to the animal with any success. The carcinomas which have been transported from one part of a human sufferer to another part of the sufferer do not elucidate the origin of carcinoma. The transportation of cancer from a human being suffering with cancer to a healthy human has to my knowledge never been successful.

We have no knowledge of what differentiates the carcinomatous cell from other epithelial cells. We only know that once the healthy epithelial cell has taken on carcinomatous qualities it possesses certain qualities that are not inherent in a healthy epithelial cell. There appears the wonderful ability to eat into and through every tissue of the human body with the exception of the hair, nails, and teeth. At least I have never heard of any carcinoma of a tooth — not even of the pulp of a tooth. There is no chemistry of the carcinomatous cell today that explains this enormous histolytic power. It may be that the lytic power is intimately associated with that other power, the power to metastasize. It may be because the cancer cell has such lytic powers and can eat its way into tissues which are ordinarily prohibited to the epithelial cell that it reaches the circulation, and, when deposited in some distant field, has the power to eat into that tissue. That difference is most striking in the case of the epithelium of the chorion. We

know that under ordinary circumstances, under conditions of health, the syncytium of the placenta eats into the mother's tissue. Particles of this syncytium can reach the maternal circulation in perfectly healthy conditions, so that we find syncytial masses in the lungs and in the liver of women who are perfectly free from tumor. On the other hand, when a woman has a malignant syncytioma, when the syncytium gives rise to malignant tumors, then the syncytial masses carried anywhere in the body form syncytial malignant tumors, though the syncytial mass of the benign syncytium looks exactly like the malignant one. It is to be hoped that chemical investigations may help us in the future.

There is one other theoretical point of the greatest importance for the success of treatment of carcinoma, and that is the question of where carcinoma ends and where allied, associated, processes begin. I am speaking of conditions which recently have been called 'precancerous.' I have never seen any report, have never seen any case myself, and have never seen any microscopic specimen which showed beyond any doubt the actual transition of benign into carcinomatous tissue. I think it is worth while to examine searchingly the foundation of this precancerous conception, which is spread broadcast, and is accepted by many in the profession. The searching examination of this hypothesis is the more important, as it is apt to form the basis for vigorous and risky forms of treatment. It has happened, in my experience, that very mild adenoma of the breast was reported to me by the pathologist as extremely suspicious. It has happened, in my experience, that a woman has had both breasts amputated and breasts examined microscopically and found free from cancer, and the woman was then congratulated by her physician that she had her breasts removed before they became cancerous. That surely is the limit of prophylaxis.

If there is such a thing as a precancerous condition, we should have some proof of it. We know there is no experimental proof, for we all know that no carcinoma has ever been produced by irritation, no carcinoma has ever been produced on the basis of induced inflammatory conditions. We are told that these conditions are precancerous, because we find them so often associated with real carcinoma. For instance, we find associated with real carcinoma in one part of the breast nonmalignant tumors in other parts of the breast. That is no proof that the one tumor is the precancerous stage which has gone on to real cancer in another area, at least it is no proof until someone has pro-

duced that change experimentally. It is almost impossible to find a cancer in the breast of a woman, of the ordinary cancer age, which is not associated with a fibro-adenomatous condition somewhere in the breast. But the reason thereof may satisfactorily be found in the great frequency of these fibro-adenomatous changes in all breasts.

The same difficulty obtains in the relation of ulcer of the stomach to cancer. I am utterly unable to find a case in my records or in the literature in which the origin of cancer in ulcer is proved. If a small carcinoma ulcerates, it is possible that the ulceration will go so far that in some areas we find only the granulation tissue. That does not prove that we are dealing with an ulcer which has become cancerous; it only proves that a carcinoma has ulcerated. The difference between a carcinoma which has ulcerated and an ulcer which has become a carcinoma is evident in theory, but the individual case may be the subject of considerable difference of opinion. Nothing but the microscope can determine the difference between benignancy and malignancy in small tumors. The necessity of microscopic examination is clear to everybody who has taken the trouble to go over cancerous breasts after removal, making sections from neighboring areas and from distant areas to find out what is going on in that entire breast.

I consider the exploratory excision with microscopic examination an invaluable aid in diagnosis, in spite of what is claimed in certain quarters — that any interference is apt to make the carcinoma worse. I have not seen any such deleterious results in my own work, and I am very prone to make such examination before doing a radical operation. I have patients who had such exploratory excisions up to 15 years ago and who are well today, after extensive operations following the exploratory excision. But I do not recommend doing an exploratory excision and then waiting a month or 6 weeks for some distant laboratory's report. The proper method is to go on at once with the radical operation, if the diagnosis of cancer is made in this way. Frozen sections enable us to make the diagnosis in the majority of cases. If they do not, the surgeon must use his clinical judgment. I am well aware that it is sometimes impossible to make a positive diagnosis on exploratory excision, that we may be doubtful for a considerable time, and in those cases the clinical judgment of the surgeon is sovereign. I warn, however, against having too rosy hopes of future advance if we begin to mix in the statistics operations for precancerous and cancerous conditions. If we were to mix precancerous cases with

the frankly cancerous ones, it will only lead to self-deception as to our results.

In our desire for success in the treatment of cancer, we have been clutching at straws and the oldest treatments have come to honor again. I refer particularly to the cooking treatment which has been applied to carcinoma of the uterus. The method advocated by Percy has been advised for inoperable and operable cases. Now we know from our pathologic work that burning out the uterus with any kind of an apparatus will leave metastatic growths in the neighboring tissues, especially the glands. As these are involved in something like 60%, that simply means to give up that number while they might be saved by the knife. To expect that the cells in the neighboring tissues, especially in neighboring glands can be killed by the heat applied to the uterus, I think is so unphysiologic that it is unnecessary to go far with a discussion in that direction.

In the last few years we have had some reports which promised great things from the use of radio-active substances, Roentgen ray, radium, and mesothorium. While we see cases of wonderful success where the carcinoma is located in superficial areas, we know that in many instances the carcinoma has grown enormously under this very treatment, and we also see that the use of the rays is apt to produce carcinoma. At any rate, so far as the deeper tissues are concerned they are useless. Kolischer has reported about 50 cases of cancer of the uterus treated by mesothorium and Roentgen ray, of which 2 are living and all others dead. I will say that all the patients with cancer of the internal organs which I have turned over to the treatment by mesothorium or Roentgen ray are dead or dying.

We hear wonderful reports from Europe of the success obtained from the Roentgen ray, radium, and mesothorium, and when we bring over the same machines they use, our patients here die. When we get such good reports from men like Kroenig, Bumm, Doederlein, and when we use the same treatment and our patients die, what is the matter? I hope we shall find out why they can do it and we cannot. We have the same people to treat they have in Freiburg and Berlin or Munich, we use the same machines which they use in Freiburg, but in Freiburg they get well and in Chicago they die.

After all is said I wish to remind you that the knife still cures its proportion of cases and that the proportion is small because the cases are turned over to the surgeon late, ruined, spoiled, too far gone. It is

still the business of every man who wants to teach students to impress on their minds that the average carcinoma case which is turned over to the surgeon in time, before it is deeply septic, before it has metastases, is a reasonably safe proposition. There is no treatment under the sun today that can show as many cases cured as the knife can. And, therefore, I say today that the success in the treatment of cancer in any part of the body that is accessible to the knife depends on the knife and the man who wields it. Until we have learned a great deal more about cancer than we now know, I think surgery is to be considered the most reliable road to success in the treatment of cancer.

OLD AND NEW ABOUT SYPHILIS

William T. Belfield
Dec. 5, 1916

Our knowledge of the bacterial infections comprises 3 phases: until about 1880, only the association of certain symptoms with certain lesions was known; during the 80's various bacteria were proved to be the exciting causes respectively of these lesions; and since 1890, certain chemical reactions of tissues infected by various bacteria have been identified.

It was obvious that the immense fund of symptomatic pathology of a bacterial disease — tuberculosis, for example — must receive sharp and critical revision, when in 1882 Koch's microscope revealed what was and what was not tuberculosis; it was equally obvious that the immense fund of symptomatic plus microscopic pathology must receive critical revision, when in 1891 tuberculin showed that the presence of tubercle bacilli in the tissues is not the whole of tuberculosis.

This critical revision by the use of the microscope showed that: (1) The infections of glands, bones, and joints previously called scrofula, are tuberculosis — surgical tuberculosis, they were later called; (2) pulmonary tuberculosis, which had previously almost monopolized this name, is a mixed infection in which the tubercle bacillus is by no means always the foremost invader. It was also learned that patients who had made a clinical recovery from surgical tuberculosis, might harbor for decades of perfect health thereafter, colonies of unsuspected tubercle bacilli demonstrable at necropsy — whence arose the sonorous epigram "once tuberculous, always tuberculous." When it was learned later that nearly every one, however spotless his record, conceals about his person colonies of tubercle bacilli, the slogan became, "Jeder hat ein bischen Tuberculose."

The tubercle bacillus bears about the same relation to different human beings as does the anthrax bacillus to different sheep — a deadly parasite to the French breed, a harmless saprophyte to the Algerian strain, with intermediate gradations.

This almost universal possession of tubercle bacilli, and the frequent inability of the microscope to detect them during life, left the clinical diagnosis of surgical tuberculosis at the primitive stage of

symptomatology, until in tuberculin we acquired an agent which reveals, not the unimportant presence of tubercle bacilli in the body, but the all-important evidence of their pernicious activity. For while over 80%, who are not clinically tuberculous, react to 10 mg. or more of tuberculin, the subject of surgical tuberculosis responds to one tenth of 1 mg. or less.

Typhoid fever is for our purpose perhaps the most instructive of the infections. The discovery of the causative agent in 1880 by Koch and by Eberth led, of course, to differentiation from typhus and other diseases clinically similar. But it did more; it showed that the organism is a deadly parasite in perhaps 5% of those attacked, but a harmless saprophyte in almost as many others, the so-called normal carriers; it proved that typhoid bacilli may inhabit the gallbladder of a convalescent for 50 years without harm to this sac, or to its owner; it proved that sensitized bacilli, inoculated subcutaneously, did not become parasites, though their activity conferred immunity.

But in this disease, also, the diagnostic limitations of the microscope became apparent, when the Pfeiffer agglutination phenomenon was applied to typhoid blood by Widal. For this revealed during life nearly all that the microscope disclosed after death — and more; notably the cases of typhoid without intestinal involvement; the persistence of typhoid colonies in certain tissues for years after their disappearance from the stools; and especially did it prove the harmlessness of such scattered colonies.

Only within the past 10 years has the immense fund of symptomatic pathology of syphilis been submitted to the long needed revision by the microscope. The spirochete enables us to recognize the chancre without waiting for the induration, which, oftener than was formerly suspected, fails to appear; it has taught us that parasyphilis is syphilis; that consumption is sometimes syphilis; that cancer of the breast may be syphilis; that the relatively noninfectious gumma contains the emasculated parasite; that the seminal fluid may convey the spirochetes — hence that the syphilitic child of a healthy mother by an infected father, gets spirochetes directly from him, not indirectly through the immune mother, as was formerly assumed; it has probably solved that hoary mystery enunciated by Colles 80 years ago, that a healthy woman, through impregnation by a syphilitic man, acquires not syphilis but immunity to this disease. Just as we acquired not smallpox, but immunity to it, through inoculation with virus sensitized in a calf's

tissues; just as Besredka's patients acquired not typhoid but immunity to it, through inoculation with sensitized bacilli; so the healthy woman acquires not syphilis but immunity to it, through the inoculation of her womb with her husband's spirochetes, sensitized by the tissues created in gestation; at least these spirochetes seem to remain localized in and near her womb, just as the immunity-giving smallpox organisms and typhoid bacilli remain localized around the site of inoculation. The positive blood Wassermann is apparently not permanent; neither is the positive Widal induced by sensitized typhoid bacilli.

Finally, thanks to the admirable work of Warthin in Ann Arbor, we have learned that men may carry colonies of spirochetes in the heart muscle, testis, or other tissues for 20-50 years, Wassermann negative as to blood and spinal fluid, and die in advanced age of nonsyphilitic diseases.

Great as are the services already rendered in syphilis by the microscope, this instrument has not solved, and obviously can never solve, some of our most urgent problems. How, and especially when, is the patient cured of syphilis? This can be answered only by some agent which detects not the spirochetes, but their pernicious activity — a tuberculin, an agglutinin, even a gonorrheal complement fixation is, when positive, convincing.

I need not argue that the Wassermann reaction does not meet this requirement, and that it bears no more specific relation to syphilis than to other morbid conditions. The negative Wassermann is now generally admitted to have no great clinical value; the earlier belief that a patient was cured because his blood Wassermann remained negative for a year, or for several years has, within my own knowledge, resulted in disasters.

Although the Wassermann fails us in a minority of cases of secondary, and a majority of later syphilis, yet a persistent blood Wassermann in the subject of clinically proved syphilis, is reasonable proof that spirochetes are still living somewhere in his body; but is it reasonable proof of clinical syphilis, requiring treatment? Not necessarily — not in all such cases. The typhoid patient always gives the Widal for weeks, sometimes for months, for years, for a lifetime after permanent convalescence is established — because scattered colonies of typhoid bacilli live in their prisons indefinitely, without appreciable harm to their host. He is permanently well, though if

we should interpret the Widal as we do the Wassermann, we should consider him permanently ill.

When 33 years old, a certain man contracted syphilis, for which he took medicine intermittently for 2 years. When 38 years old he married; his wife had no miscarriages but gave birth to 3 healthy children who are now vigorous young adults. The father, now 66 years old, is exceptionally robust; he has had no treatment for syphilis, no recognized symptoms of the disease, and no serious ailment for 30 years. During the past 6 years I have had 8 blood Wassermann tests made, 6 of which proved distinctly positive. His wife and elder son give negative Wassermann tests; the other children have not been examined.

This case, and others essentially similar already on record, must be pathologically identical with the typhoid Marys and gonorrheal Tommies, in that the tissues and the parasites live in mutual tolerance indefinitely. It is conceivable that these may ultimately be found to constitute a considerable percentage of those infected with syphilis.

At its inception, bacterial pathology assumed two postulates: (1) The healthy man harbors no pathogenic bacteria under his skin; (2) the invasion of subcutaneous structures by such bacteria means a fight to a finish, which finish, if the host survive, consists in the destruction of the invaders, leaving the tissues in their pristine purity. This conception did, indeed, fit accurately the only bacterial disease that had been thoroughly studied prior to the 80's, namely, the anthrax of sheep and cattle.

Today, the fruits of 35 years' research compel us to revise this early conception, and to recognize that convalescence, while achieved in some by destruction of the invading organisms, is secured in others by their imprisonment; in the latter event, the prisoners may be slowly and finally destroyed; or they may survive as harmless captives during the life of the host; or they may sometimes escape from jail and again give battle.

Thanks to the microscope and to biochemistry we now know that such are the actual issues of the conflict between human tissues and many bacteria, notably the tubercle and typhoid bacilli; and we have every proof, except those requiring a specific chemical test, that convalescence from syphilis also is achieved not only by the destruction, but also by the imprisonment of the invaders. A recognition of this parallelism — clinical, pathologic, serologic — between tuberculosis and

typhoid on the one hand, and syphilis on the other, is, I think, forced on us by the recent developments in syphilology, to which I have briefly referred.

For these reasons I am not of those who believe that tuberculosis or syphilis is of necessity, and always, an incurable disease, and who dolorously cry "once tuberculous, always tuberculous; once syphilitic, always syphilitic," because scattered colonies of imprisoned tubercle bacilli or spirochetes may be found after death from other causes, and after decades of robust health; for these colonies I interpret as the vanquished, not the victors, in a bygone struggle; even though the excreta from their prisons maintain a persistent tuberculin, Widal, or Wassermann reaction.

On clinical grounds we know that spirochetes, imprisoned for years, have in many instances escaped from their bounds; but how numerous are those others who have no relapse? No one knows; but no reasoning man bases his estimate of marriage as an institution solely on divorce court records.

On the other hand, until we procure a means for proving the total absence of syphilis, we shall be unable to say to any given patient, "You are cured."

On my own patients who have apparently recovered from syphilis, I impose two injunctions: (1) Many syphilitics recover permanently, others do not. To which class you belong, I do not know, and can not ascertain. You renew every year your insurance against possible injury through accident; I enjoin you, to renew every year your insurance against possible injury through syphilis. (2) Should you ever be afflicted with any obscure or chronic ailment; should your health ever fail without obvious cause, I enjoin you to tell your physician promptly that you once contracted syphilis.

If you will faithfully observe these two injunctions to the end of your life, you may then, with full confidence, direct that your tombstone be adorned with the triumphant legend, "Cured of Syphilis."

THE NATURE OF COHESION

A. P. Mathews

Jan. 25, 1917

My interest in the subject of cohesion arose from a study of surface tension. It is the opinion of most biologists that surface tension is one of the most important physical facts in the constitution of living matter. It is the tension of the liquid surfaces within the living matter which is supposed to determine all kinds of vital activities. Surface tension is a function of molecular cohesion and before we can understand this tension we must understand cohesion. By cohesion we mean the attraction of molecules for each other. But cohesion comes into play or may come into play in other phenomena. For example, what is the nature of the attraction of sperm nucleus for female egg nucleus? The two come together. Is the attraction which draws them together due to cohesion? In looking into this matter I was surprised to find that while the laws of gravitation were pretty well known and that while the attraction of atoms, or chemical attraction, was partially understood, nothing was known about the nature of cohesion. It is not known what it is in a molecule which determines the power of its cohesion, nor is it known what the law of attraction is. Is the attraction inversely as the square of the distance, or inversely as the 4th, 5th, 7th, or other power? No one knows. All that is known is that ordinarily for some unexplained reason the attraction extends but a very minute distance from a molecule, but whether this is due to the absorption of the molecular lines of force by the ether, or by other molecules, or whether it is due to some other cause is not known.

The principal and one of the earliest workers on the subject of cohesion was a physician. Perhaps that may justify me in bringing it before you. If it interested so greatly that other physician, I may hope that you also will find it of interest. This man was Thomas Young, the great English philosopher, he who discovered the structure of the crystalline lens of the eye; who gave us the theory of color vision; who first explained accommodation of the eye and astigmatism; who started the translation of Egyptian hieroglyphics, and who also more than another aided in the establishment of the wave theory of light by the explanation of interference phenomena. It was he also

who first explained the nature of capillarity and connected it with molecular cohesion. In his classical papers on this subject he made the first true estimates of the approximate sizes of molecules and the amount of their attraction to each other. He did all this while he was also a practicing physician, attached to a London hospital.

I have found several ways of determining the amount of cohesion in liquids and gases. I shall not describe these methods but shall state only that we may compute the cohesional attraction of molecules from the deviation of gases from the ideal gas laws; from the surface tension; from the latent heat of vaporization; from the pressure of a gas when it is heated at constant volume, and from the critical data of a liquid or gas. I have computed the mass factor of the cohesional attraction, that is, the cohesional mass of the molecules, which corresponds to their gravitational mass, by these different methods for about 50 different kinds of normal substances. The substances are of a great variety of kinds. They range from the elements such as hydrogen, nitrogen, oxygen, and such simple gases as CO, CO_2, N_2O, SO_2, Cl_2, Br_2, through CH_4 to octane, C_8H_{18}; they include such esters as methyl butyrate, and such inorganic substances as stannic chlorid.

Having determined the cohesive mass of each kind of molecule, the question arose as to the elements in the molecule which determined the amount of its cohesion. One of these factors is the molecular weight. The heavier molecules have the more cohesion. I have discovered that the other factor is the number of valence electrons in the molecule. I discovered that the cohesive mass may be calculated for any molecule from the molecular weight and the number of valence electrons by the following formula: $a = N^2 \, (m^2k \times Val/M)^{2/3}$. In this equation a is the cohesive mass; it is a of van der Waal's equation; m is the gravitational mass; k, the gravitational constant; N, the number of molecules in the volume of gas or liquid; Val, the number of valence electrons, and M, the molecular weight. The values of a computed by this formula have been tabulated side by side with the values calculated from the surface tension, the latent heat of vaporization, from the deviation from the gas laws, and in others ways. The excellent agreement is apparent.

The fact that the cohesion is thus shown to be a function of the number of valence electrons in the molecule, these being electrical in nature, and of the molecular weight, clearly indicates that cohesion is of the nature of magnetism, if indeed magnetism is not identical with cohesion.

THE APPLICATION OF SOME PHYSICOCHEMICAL METHODS TO MEDICAL PROBLEMS

Shiro Tashiro

Jan. 25, 1917

There are two types of contribution that physicochemic science makes to the field of medical science. The first type consists of the analysis of complex biologic phenomena in the terms of physical chemistry and the interpretation of these data in physical language. This form of application makes possible the formulation of the biologic phenomena according to well-known physical laws. It creates quantitative laws in the medical sciences. A good example of this kind of contribution is the book recently published by Arrhenius entitled, "Quantitative Laws in Biological Chemistry." Nernst's theory of the nerve impulse furnishes a good example of the power of an idea presented by a physical chemist to hold the mind of a biologist.

An an illustration of this type of contribution, I should like to consider, first, the theory of anesthesia. There is no subject in medicine, I believe, that has attracted more attention than this one. The practical and theoretical importance of the phenomenon of temporary suspension of the tissue irritability has demanded the attention of practically all branches of science. The contributions of physical chemistry to this problem are numerous, but the most recent one is an attempt to explain this phenomenon on the theory of surface tension.

Troube points out that isocapillary points of all important anesthetics produce all the same typical anesthesia; that is, if one selects different concentration of the various drugs in such a way as to lower the capillary rise of pure water to the same point their anesthetic power is found to be the same. Thus the property of lowering surface tension is thought to be the primary function of all anesthetics in producing anesthesia, probably through the lowering of the internal pressure of the cell and the consequent change in the state of colloidal aggregation within the cell. A change in tissue oxidation, if there is any, may be merely a secondary phenomenon produced by important primary physical changes.

There has also been an effort to show that several typical anesthetics can act on certain fertilized eggs, practically without interfering with

the normal oxygen-intake of the eggs. However, before we accept any theory of anesthesia we should, once for all, determine whether or not the tissue metabolism can go on without interruption during narcosis. For this we should study carbon dioxid-production rather than oxygen consumption, for it is a well-known fact that some organism or tissue, which does not depend on atmospheric oxygen for respiratory activity, can nevertheless be easily anesthetized. It is also more satisfactory to study the metabolism of the nerve than the fertilized egg, because in the former we do not produce any visible functional structural changes by narcotics, thus eliminating all the possible, physical effects which we usually produce in the case of the fertilized egg—a change which in itself might be capable of producing a typical lowering of metabolic activity.

For this examination we used the biometer, an apparatus which can measure carbon dioxid in one-tenmillionth of a gram. By direct determination of the gas under anesthesia in the nerve fiber we found the following interesting results: If we take an anesthetic like chloral hydrate or ethylurathan in the concentration which produces the reversible loss of irritability of the nerve, we find that the carbon dioxid-production is less than half the normal production. In other words, one cannot produce narcosis of the tissue without interfering with the tissue metabolism of the nerve; the same is true of the fertilized egg.

If we take a weaker concentration of anesthetics which we know produces a primary stimulation of the nerve, we find a corresponding increase of carbon dioxid in the nerve. So I do not believe that we can accept a theory that narcosis is produced by purely physical processes and that it has nothing to do with tissue metabolism. I should like to point out here a very common source of error which some investigators have failed to take into consideration.

If we compare carbon dioxid-production from 2 nerves of the same size, one of which was left in 0.4 per cent. chloral hydrate, and the other in sea water for 5.5 minutes, we find that the treated nerve gives off much more carbon dioxid than the normal. If we measure carbon dioxid-productions from these nerves after 15 minutes, the treated nerve still gives a higher production of the gas; but after 1 hour, the treated nerve produces far less than the normal one. I may add that the claw nerve of spider crabs, which we used, becomes more excitable when treated in this concentration for a very short time, but after 1 hour or so complete anesthesia sets in. Evidently it is of prime

importance to determine the carbon dioxid-output for a comparatively small interval than for one of long durtation. If we determine the carbon dioxid-output for 60 minutes' respiration of the nerve treated with 0.4 per cent. chloral hydrate, it is quite obvious that we might be led to an erroneous conclusion that the narcotics have no effect whatever on the metabolic rate. For the nerve during a primary stimulation by narcotics respires more than the normal, while at complete anesthesia its rate is less than half that of normal, and the algebraic sum of these 2 results might readily approximate the value found for normal carbon dioxid-production.

Although there are still possibilities that such interference of the metabolic activity of the tissue under narcosis may be due to some primary disturbance of structural balance in the tissue, yet I wish to make 1 point clear, namely, that there has as yet been no really good reliable work done which shows conclusively that tissue metabolism is not interfered with during narcosis.

I have been often asked what would be the use of our endeavoring to decide which are the more important changes in the tissue during narcosis, chemical or physical, since a fundamental demarcation between physical and chemical reactions is not so marked after all even in the pure physical and chemical sciences. I wish to defend this plausible objection with a general scientific principle, that is, it is of practical advantage for us to know this for experimental procedure and application. Whether we take the chemical view or not, the mere fact that the nerve respires differently according to its state of irritability gives very interesting criteria for several other studies in medical science. With the quantitative method on the rate of carbon dioxid-production, we can study other allied subjects. An illustration will make this point clear.

We found, with our apparatus, that not only are there different rates of metabolism among different kinds of nerve, but that ths rate of metabolism along the same nerve is unequal. I can generalize this by saying that the nerve fiber which is nearer the source of the natural stimulus has a higher rate of metabolism than the portion away from it. In other words, the afferent fiber has a greater chemical activity at the peripheral portion, while the efferent fiber has a higher metabolism at the portion nearer the brain. This law holds both for axis-cylinder or sensory dendron. So far we have found no exception.

Now this metabolic difference is quickly abolished or reversed by

the use of narcosis of different concentrations. In general, the more metabolically active the portion is the quicker it is to suffer its anesthetic effect. Thus even the same anesthetic of the same concentration acts differently on the same nerve if the metabolic rates are different. I believe it is very probable that a drug like cocain might pick up the sensory ending first, not so much as a specific action of the drug on the particular nerve, but probably because its metabolic rate is quite different from the rest of the nerve. Many other phenomena such as degeneration and regeneration might be similarly explained, at least partially, on the metabolic basis. Only accurate quantitative experimentation will test these hypotheses regardless whether or not anesthetics act on the tissue or on the respiration first, or whether the disturbance of respiration during narcosis is a subsequent factor due to other primary physical changes.

The 2nd type of contribution consists of the application of physicochemical methods to medical science. It is a very highly developed exact technic of chemistry of which we make use in examining the clinical material. We daily accummulate many so-called physical constants of normal and pathologic body fluids, such as viscosity, H-ion concentration, refractive index, surface tension, osmotic pressure, electrical conductivity, freezing point, isoelectric points, vapor pressure, and so one. Such constants are annually collected in the biological section of the "International Table of Physical Constants." We believe that this type of contribution brings us much closer to the application of physical chemistry to medical science.

As an example of this sort of application, I may mention some work Dr. Levinson and I have been doing in an effort to differentiate spinal fluid of tuberculous meningitis from nonmeningeal fluid, and also from fluid of epidemic meningitis. We took as our basis the hydrogen-ion concentration and the protein content of the spinal fluid. Since the reactions of the fluids differ with different pathologic conditions, we thought we could, in this way, distinguish one condition from another by examining the bahavior of the protein content.

All protein we know is disassociated into electrically charged ions. The disassociation of protein, however can be changed by adding either acid or alkaline to the solution. When acid is added the main part will become positive; when alkaline is added it becomes negative. Therefore when wishing to precipitate a protein in an alkali, one must

have a positive metal to precipitate it, and when the protein is in an acid solution one must have negatively charged ions to precipitate it.

Acidulated gelatin is put in a cataphoresis tube and picric acid in the 2 arms, an electrical current is passed; there will be a heavy precipitate at the cathode; gelatine with alkali, on the other hand, goes to the anode. The negatively charged picric-acid ions react with the positively charged gelatin which moves toward the cathode. The fact that gelatin moves to the anode in alkaline solutions can be shown similarly by using positively charged ions like mercuric and copper instead of picric acid.

Both tuberculous and epidemic meningitis contain large amounts of protein, but quantitative estimations alone cannot distinguish them from each other. But if the H-ion concentrations differ, we might be able to show it in the cataphoresis tube. In fact we found that fluid of a tuberculous meningitis goes to the positive pole, showing that there is more negatively charged protein in the spinal fluid. On the other hand, we found that fluid of an epidemic meningitis goes to the negative pole. We can thus distinguish tuberculous meningitis from normal by the fact that the fluid of tuberculous meningitis shows a heavy precipitate on one side, whereas, that of normal condition shows merely a diffusion. We can differentiate tuberculous from epidemic meningitis by the fact that the fluid of the former goes to the positive pole, whereas that of the latter goes to the negative pole.

For example, we had in our work a case which was not suspected to be tuberculous meningitis, but in the cataphoresis the protein went to the positive pole; shortly afterwards we learned that the child died of tuberculous meningitis. We had another case, incorrectly reported as tuberculous meningitis, the protein of which did not go to the positive pole. That patient, we learned later, recovered. The most serious exception came up in a case in the Sarah Morris Memorial Hospital which was reported as epidemic, but the fluid of which went to the positive pole, and we could find no explanation for the action.

We can also show the different behaviors of protein in different fluids without passing them through a current, that is, by precipitating some protein with acid precipitants and alkaline precipitants, and comparing the sediments with each other.

Our work is still in the experimental stage, but we present these facts to show the possibilities of the application of physico-chemical methods to medical science.

DISCUSSION

A. P. MATHEWS: I wish to speak briefly of some results obtained by Dr. M. L. Menten on the hydrogen-ion concentration in the blood in cancer and other conditions.

It is probably known that the determination of the H ions in blood in disease has not given very definite results. Variations are found in normal persons fully as great as those reported in pathologic states.

Dr. Menten was struck by the singular fact that various samples of blood drawn from different patients on any day showed just about the same concentration of H ion, whereas on different days they would all vary in the same direction. At first it was thought this might be due to temperature, but these were all patients in the hospital in much the same temperature. It was run down finally as due to barometric pressure, which is to me a very interesting thing. If the barometric pressure is high the alkalinity of the blood is increased, and less alkalinity and more acidity occur with the lower pressure. One would expect just the reverse of that from the carbon dioxid pressure. It makes me think that there is something in the old notion of rheumatic people that they can tell the change in the weather by the feeling in their bones. Dr. Kyes who had a bad attack of arthritis, once told me that he felt sure that he was a good weather prophet and he tried to find out what it was in the atmospheric conditions to which he responded. The only thing he could find was the barometric pressure. It is possible that bearing in mind the fact of variation in alkalinity with barometric pressure one may find significant variations in alkalinity of the blood in pathologic conditions, a thing which has hitherto been impossible. It has been said that a condition of acidosis often occurs at high altitudes, which accords with Dr. Menten's results.

The other condition is the alkalinity of the blood serum and it is a very interesting observation that in nearly all varieties of cancer—Dr. Menten examined about 70 cases—there is a decided increase in the alkalinity of the blood serum. In a normal person a variation in Ph is found, from 7 to 7.9, that is. the H ions vary from $N \times 10^{-7.2}$ to $N \times 10^{-7.9}$. In all except a few cases of cancer of the lip, the serum alkalinity was much increased. Particularly in cancer of the stomach the alkalinity was high. Dr. Menten was able to correct one or two diagnoses which were erroneously made by finding that the alkalinity of the serum was normal, and subsequent examination showed that the wrong diagnosis had been made and there was no malingnancy. In another case where it was impossible to tell whether there was an internal growth, the alkalinity of the serum enabled a positive diagnosis, which was confirmed by operation. In few other diseases was the alkalinity of the serum found to increase.

In syphilis the serum is normal. In diabetes the serum is more alkaline and the Allen treatment increases this alkalinity. In pregnancy the alkalinity is normal, which is interesting in that the rapidly growing child does not affect the alkalinity of the mother. In rheumatism and chronic endocarditis particularly the acidity is much increased in the serum. Dr. Menten investigated one or two other diseases which also gave a high alkalinity. I think the increased alkalinity of the blood in cancer may have some significance. It has been found in the development of eggs that an increase of alkalinity of sea water produces a stimulating effect on speed of development. In cancer this increase in alkalinity may be of importance in determining the rapidity of growth and it may be of some diagnostic value.

J. H. LONG: Were the reactions for the serum or for the whole blood?

A. P. MATHEWS: The last was of the blood serum but the barometric pressure alkalinity was that of the whole blood.

J. H. LONG: The increased barometric pressure would facilitate holding a larger amount of oxygen. Would that not have the effect of decreasing the H ion concentration?

A. P. MATHEWS: I think not, because if it did it would have the same effect with the serum. The hydrogen on the electrode could be changed but the blood alkalinity not affected. The findings relative to cancer were based on 70 cases. The work was done in the Skin and Cancer Hospital in St. Louis.

J. H. LONG: I think it might be useful to some who are working with hydrogen to know that I found it possible to get very usable tank hydrogen. I procured it from a firm of manufacturers and there was no oxygen left in it, or only a small part of 1%, which did not interfere with its usefulness. Of course it had to be washed, but I found it very satisfactory.

PSYCHANALYSIS AND THE PRACTICE OF MEDICINE

William A. White
WASHINGTON, D. C.
March 30, 1917

The most difficult concept to grasp is that our psyche bears within itself the records of its hundreds of thousands of years of evolution and development just as does our body. Just as the body has remnants of a tail and of gill slits which bear silent testimony to the path along which it has travelled to reach its present estate, so does the psyche bear similar evidences of its origins; and just as the body in its development has brought into its present structure only these vague reminders of its past, but is what it is today only because of that past, so the psyche, while it, too, contains vague reminders of what has been, is what it is only because of its past, a past on which the present has been constructed. This past, the historical past of our psyche, is always growing for as soon as the material of the present has been used as material in our growth, as soon as it takes its place in the path of our development by being used as a resting place for further superstructures, then it enters into our historical past. This is the unconscious.

THE UNCONSCIOUS

As man has developed he has had progressively to give up more and more of his primitive, instinctive tendencies as the price for a higher civilization with all of its inestimable benefits. As these instinctive tendencies have been overcome, they have been relegated to the unconscious; and out of the successes attained in the overcoming have been forged the weapons with which to win a new victory. That these cravings have been overcome and buried in the unconscious does not mean that they have ceased to exist or that they have ceased to be able to influence the individual. Like long forgotten events that a chance association brings flashing into the memory, they may be stirred to activity at any time; or, forgotten and apparently nonexistent they may nevertheless exercise a continuous but subtle effect on the conscious activities. The poet Grillparzer ceased to be able to write poetry

at 28 following the suicide of his mother. He was in the midst of his composition the "Golden Fleece." He picked up the thread of his lost art again, however, on the occasion of playing Mozart's Symphony in G minor with a mother substitute, a woman who reawakened his mother associations. This was the last piece he had played four-handed with his mother before her death,[1] and so served to give him access again to those sources of energy which had been cut off by her death.

In the unconscious, then, we find the instinct motive for conduct, which is the motive of the familiar, the usual reaction (habit), the easiest way, in short the pleasure motive. At the level of clear consciousness reason and judgment hold sway; here the motive is the reality motive, a clear-cut, conscious, intelligent relating of the individual to the facts of existence, which involves, among other things, impressing of instinct in the service of reality and therefore effort, work. Psychanalysis is essentially a study, by a special technic, of the unconscious for the purpose of learning the part the instinctive motives play in the life of the patient. In the words of Freud:[2]

> Psychanalysis originated on a medical basis as a method of treatment for certain nervous maladies which are called functional and in which there is recognized with constantly increasing certainty the result of disturbances of the affectivity. It attains its object of removing the expressions of such disturbances. the symptoms, by presupposing that these symptoms may not be the only possible and final outcome of certain mental processes, and with that in view, exposes the history of the development of the symptoms in the memory, re-awakens the processes lying underneath these symptoms and affords them a more favorable outlet under the guidance of the physician. For, today, we know that the pathological symptoms are often nothing else than substitute formations for bad, i. e., unsuitable, tendencies, and that the conditions of the symptoms are established in the years of childhood and adolescence—at the same time in which the individual is the object of education—whether the maladies actually appear in youth or only in a later period of life.
>
> Education and therapy now appear in a reciprocal relation to each other. Education will take care that from certain dispositions and tendencies of the child, nothing harmful to the individual or society shall proceed. Therapy will come into play if these same dispositions have already caused the unwishedfor result of a pathological symptom.

Here is the key to the situation. An analysis is for the purpose of reconstructing the psychologic history of the patient so far as that history bears on the formation of the symptoms. As soon as we do this we invariably find that the symptoms represent, symbolize, a form of instinctive activity which belongs to the period of infancy and should

[1] Pfister: The Psychoanalytic Method, 1917, p. 120.
[2] Ibid., p. 5.

have been renounced as the child grew to adulthood, but which, because of some special emphasis it then received, has been retained. Common examples are the difficulty with which some children give up the bottle, and in adults the habit of nail biting which has been carried over from infancy.

In both of these examples it is quite evident that the activities give pleasure and also that they should be renounced. In other words, they are infantile. They are both interesting, too, as belonging, the first to a real, the second to a symbolic nutritive or self preservative activity, as opposed to a plainly sexual or race preservative form of activity, these being the two forms of expression into which all others are ultimately reduced. The implication is that a given person may retain evidences of his infancy only in certain zones of his conduct, the gastro-intestinal, mount, ear, eye, skin, genital, or other zone. These are the so-called partial trends. If the tendencies of the individual as a whole, that is, all of his energies be called by a single name, we may use the term libido, then these partial manifestations would be called partial libido trends.

THE LIBIDO

An analysis of the patient will disclose, then, that one or more of the libido areas has remained at its infantile level of development, has retained its infantile ways of instinctive reaction, of pleasure seeking, has refused to grow up or, to sum it all up, has failed to socialize its libido. That is, it has failed to use some of its energies to the larger ends. As an example of such infantile and social ways of using, let us take the ear libido. From the standpoint of the usual social evaluation, the type of person who is always listening to hear scandal of his associates is despicable. He does not listen to hear something good but always to hear something bad, and the worse the better. This is a somewhat less obvious pleasure-seeking device than that of the person who is all attention at the telling of every obscene story; but the principle is the same because it is the obscene that he is really listening for. Such a person is a pedler of gossip, a besmircher of reputations, and in all sorts of ways, at the level of ear libido (listening) an asocial, destructive member of the community and incidentally a very unhappy and unfulfilled person himself. As far as his function of hearing is concerned, he has not grown up. He is still using his ear to minister to a low level type of curiosity. His ear has not been adequately integrated as a part of a socially useful member of society, and therefore

is not used to further socially useful, constructive ends. It remains at the instinctive, pleasure-seeking level. How much better he could use his proclivity to listen by going to lectures, readings, or concerts and thus socializing his trend by using it for bringing him into contact with his fellows at socially useful levels.

PSYCHOGENIC DISORDERS

Before discussing such character traits as this, though, let me read a list of psychogenic disorders culled from recent writers who were practitioners in various specialties, not psychanalysts, for the purpose of emphasizing the interest in the psychogenesis of apparently physical disorders which has recently arisen, and also because many or most of these ailments would be apt at least to be treated by other than psychologic methods. This list includes many forms of asthma, sore throat, difficult nasal breathing, stammering, headache, neurasthenia, backache, tender spine, "weak heart," fainting attacks, exophthalmic goiter, aphonia, spasmodic sneezing, hiccup, rapid respiration, hay-fever, gastro-intestinal disturbance (constipation, diarrhea, indigestion, colitis, gastric ulcer), ptosis of kidney, diabetis, disturbances of urination (polyuria, incontinence, percipitance), menstrual disorders, auto-intoxication (from long continued digestive disturbances), nutritional disorders of skin, teeth, hair, etc. The list might be indefinitely prolonged. Let me only briefly add examples of apparently physical disorder for purposes of illustration.

Of the vasomotor disorders I cite the case of[3] a 15-year-old girl who during analysis exhibited swollen lips. This had occurred once 5 years before when a student had tried to kiss her but she had successfully resisted him. A similar attempt had been made before the later recrudescence of the symptoms.

An example of a skin eruption is the case of a young woman[4] who had areas of erythema on both forearms. These areas did not tan on exposure to the sun as did the rest of the skin. Analysis showed that the erythematous areas were the places which had been grasped by the mother-in-law in a very emotional scene between them. The erythema disappeared following the analysis and the skin in that area then tanned on exposure.

Certain cases show well that disturbances of menstruation, dysmenorrhea, and suppression may be purely psychogenic, due often to a

[3] Pfister: The Psychoanalytic Method, p. 32.
[4] Personal Communication from Dr. E. J. Kempf.

timid, prudish, neurotic mother who scares her daughter to death over the onset of the new function, or leaves her in ignorance to conjure up her own fears on its appearance. Subsequent local treatments, curettage, ventral suspension, etc., not only may not help but may aggravate the anxiety, make the patient decidedly worse because, of course, they do not go to the root of the trouble but only deal with results.

I have cited these examples for the purpose of showing that psychogenic disorders are by no means confined to such types as the familiar hysterical aphonias and hysterical palsies, with which all are perfectly familiar and which are easy to recognize. On the contrary, they frequently produce disorders much more subtle in their manifestations, and what is more, may involve not only deep seated character defects but also metabolic disturbances in which we are not accustomed to look for signs of psychic causation, for example, visceroptoses caused by psychic disturbances, depressing emotions, acting by way of the vegetative nervous system.

Even, however, in instances of such evident hysterical reactions, the mere dealing with the symptom and causing it to disappear is a very inadequate treatment, for it does not touch the underlying trouble; it leaves the character defect as it was, only, as a rule, to manufacture new symptoms. A boy of 17 had for some days a strange feeling in his left arm. This feeling was contemporaneous with the desire of his father to take him from his present school and send him to another. The boy did not want to go. Analysis revealed the fact that when as a child he was about to be vaccinated he struggled so violently that he succeeded in avoiding the disagreeable experience. This experience was entirely unknown to the patient until brought out by analysis.[5] The interpretation becomes easy if we will use the formula for such cases. The symptoms mean a wish that things might be "as they were then" on that other occasion when they tried to vaccinate him. That is, he wishes that he may succeed, by his obstinacy, in thwarting the desires of his father as he succeeded before. The treatment of such a condition by causing the disagreeable sensation in the arm to disappear by suggestion on the theory that that is the disease can at once be seen to be entirely inadequate to the situation. It leaves untouched the character defect which is to react by obstinacy to disagreeable situations. In this respect the boy is retaining an infantile way of

[5] Pfister: The Psychoanalytic Method, p. 44.

dealing with things he does not like, and needs to be helped to grow up, to develop on this side of his character. Unless the treatment is directed to such ends, it misses its goal.

PRACTICAL PSYCHOLOGY

The difficulty has been, in the past, that psychology has never employed itself with such questions. Entrenched in its laboratories, it has carried on its work far removed from the everyday life of "the man in the street." But now that is exactly what psychanalysis is demanding of it. Why John Smith does not get along with his wife has always been a matter of absorbing interest to the neighborhood, but psychology has never dignified such a problem with its attention. It is through just such facts, however, it is because we do not get along with our wives, because we are not interested in our work, because we are not appreciated by our chief, or are imposed on by our associates, because we get too tired, sleep too little, drink too much, because our salary is too small, or we can not save, or the other fellow who does not do as good work as we do gets more, or a thousand other reasons, none of which for a moment cause the sufferer to seek the advice of a physician, we are finally coming to see that it is just such things as these that make the difference between a happy life, filled with usefulness, and failure. Of such problems from the point of view of the educator Pfister says:[6]

> Of the analytic educational work with pupils, who, without being really ill, still because of inner inhibitions, make themselves and their families unhappy, there is almost no mention anywhere. How the hitherto unobserved impressions of childhood control the whole later development of the normal individual, even to the peculiarity of his style, his choice of a vocation and of a wife, as well as the most insignificant subordinate affairs, finds too little discussion. The enormous loss of love for fellowmen and of power for work which many individuals suffer, mostly without knowing it, as a result of unfavorable educational influences, have not, up to the present time, been given their proper weight in the literature. . . . Countless numbers of persons who bring heartbreaking grief to their parents and other people and cannot help bringing it because they are under neurotic obsessions, can by the aid of analysis be changed into agreeable, useful individuals.

Unless psychology is willing to busy itself with such problems it may well be called on to justify its existence.

Psychanalysis is essentially an educational procedure. Its object is to clear away the rubbish which is obstructing the pathway of the patient so that he may have a chance to go forward. This is precisely

[6] The Psychoanalytic Method, p. 14.

what education tries to do. Most emphatically neither should try to impose ideas on others; they should simply make the way free to permit the fullest development of the personality.

HEREDITY

It is, of course, the fashion in some quarters to emphasize heredity as the responsible agent for all childhood anomalies and deviations from later normal development. This is surely the easier way. The cry of the eugenicists for sterilization laws reminds me of the Queen of Hearts in "Alice's Adventures in Wonderland" with her "Off with their heads"—a simple solution and seductive, but like all such things, too easy. We find that we must really come back to a constructive program that involves work, the expenditure of effort, if anything of value is to be accomplished.

The psychanalysts believe there are shorter cuts to the neuroses than by way of heredity. Here are a couple of remarks by parents which recently came to my attention: One mother says that a child has no morals until after 9 years of age. Before that they are just little animals and so, of course, there is nothing to do about it—a fine formula to relieve the parent from all responsibility and sanction a program of donothingness. Another parent believes in teaching children absolute obedience—a fine thing for the parent surely, but what of the child? How can one expect a child in either one of these households to develop? How is it going to be possible to get any chance at all? As a result must it not almost surely happen, that, thwarted in his natural avenues of expression, he will seek the by-ways? That is the stuff out of which the neuroses and future inefficiency and unhappiness are built.

I cannot refrain from mentioning a recent experience. A woman of very splendid qualities but with certain childish reactions of a difficult, surly, inaccessible type, which were wrecking her happiness, had all sorts of difficulties with her little boy. She and he were in constant conflict. One day, towards the end of the analysis, she came to me with this incident: She was busy with some photographs when the little boy came in the room. He at once started to make things rather lively whereupon she said, "Now my dear, if you will be quiet you may stay with mother." This was an altogether new reaction on the part of his mother, and so he responded by saying, "Really, mother, may I stay?" She answered in the affirmative and he proceeded to compose himself

and became interested in the pictures; but before finally sitting down, by way of reassurance, looked up and said, "Really, mother, do you mean it, may I stay?" A response of love had been met in kind, and when the analysis was completed she and her little boy were rapidly getting on a basis of real friendship and comradeship.

These illustrations show clearly that it is often not the apparently sick person who needs the attention. As in the case of these children, for example, it is often of much more importance to straighten out the mother; without that it might well be impossible to help the child materially. The lesson from such cases is that the field of medicine is broadening tremendously. We are on the verge of admitting all sorts of problems which a generation ago we did not even know existed. The problem of psychanalysis is such instances as these has to do not only with the individual who may come or be brought to the consultation room, but also with the whole family and their social setting. Its breadth of application is sufficiently evident without further elaboration.

From the cases thus far adduced it will be evident that the theory which accounts for the later neurosis assumes that the trouble began in the early years of childhood, not as the result of some concrete sexual trauma, as many people still think, but as the natural consequence of a fixation of certain areas of the child's interest, so that in this particular respect he does not grow up. The cause of this fixation, which, for our present purposes, we may call detention of the libido or interest on the road of development, is that the child's interest is too strongly attracted because of the undue pleasure premium which this particular area of interest offers. In the case of the asocial ways of using the ear libido already mentioned, for instance, it would probably be found that the child was early attracted to listening ways of pleasure seeking because of having heard or been told about forbidden sexual matters that he found absorbingly interesting. Only by finding such things in the history can the later development be understood. That the matter was sexual is ventured only because that is what would be expected from experience. That all pleasure founds in the last analysis in sex pleasure is an hypothesis forced on the analyst by his daily experience; it is not an arbitrary hypothesis into which he tries to make every fact fit. The hypothesis that all pleasure, in its ultimate analysis, is reducible to that quality of emotion which is associated with the most important act in the life of the indi-

vidual, from the point of view of the welfare of the race, is not a whit more surprising or more radical than the generalization that all of the attributes of life are traceable to the single property of protoplasm—irritability. After all, it is of less practical importance to answer the question "Whence?" than to answer the question "Whither?" It is only a matter of detail how we reply to the query "Whence?" for in any case we have all traveled the same evolutional pathway. To the individual, however, it is of the greatest importance that he should be able to make the best use of his opportunities, that he should be able to answer the question "Whither?" in a satisfactory way. But there is another aspect of the matter which I think of especial importance.

All along the biologic pathway progress has been possible only because each unit, besides preserving its own integrity, has been willing, so to speak, to give something to the larger unit of which it formed a part. Each cell, besides preserving its own life, must give up part of its activities to help in the activities of the organ of which it is a part; the organ must do likewise with respect to the larger unit, the individual and the individual must repeat the process as a member of society—the herd. The liver, for example, besides preserving itself as a liver, stores up glycogen to be used by the muscles when the individual is in danger, and gives of this store for the larger whole; the man pays his taxes and similarly helps to problem of society, of which he is an integral part. It thus comes about that in the process of the successive integrations to progressively larger ends, what we call personality or character issues as an end-result, depending, however, on all those bodily processes which underly it. Therefore, according to Adler, character traits ultimately are reducible to terms of organic structure, and so defects of character depend on organ inferiority.

ADLER'S THEORY

The adlerian concept would substitute for the freudian theory of 'libido fixation' as an explanation for a given defect of character the theory of an inferior organ. He believes that an inferior organ gives a sense of insecurity, inferiority, against which the neurotic tries to protect himself by so ordering his life, so regulating his every act that he may find that security of which the feeling of inferiority has robbed him. This effort to find security is the fictitious goal of the neurotic who fails in attaining the maximation of his ego because his efforts are

directed along this false path. He is not free to deal with reality at his best, but must always subordinate the demands of reality to the inner need of satisfying his craving for security. The neurosis or psychosis is therefore a constructive creation, a compromise, a compensation product, which, however, fails because of its false direction. His theory, summed up in a few words, reads: The neurotic constitution founds in an inferior organ; the inferior organ produces a feeling of inferiority; the feeling of inferiority creates the fictitious goal of the neurotic, whose symptoms result from an effort to mold reality along the false pathway that leads to safety.

From this point of view our asocial listener would receive a somewhat different interpretation than we have thus far given, namely, it would be expected that an examination of his ears would show that they were in some way inferior organs. In confirmation of this I may say that in an examination of a number of sense organs in hallucinated patients I never found one what could be considered a normal state.[7] Let me add as serving to bring the adlerian and the freudian theories together that Adler asserts that wherever such organ inferiority can be demonstrated he has never failed to find also an inferiority of the sex organs.

To come back to our listener: Not only should we expect him to show inferiority of the organ of hearing, but also we should expect him to feel a sense of inferiority which would manifest itself in the zone of ear libido. We might expect him to feel frightened, for example, if he was unable to hear what people were saying and consequently to feel that they might have been saying something about him, something not pleasant, of course, hatching up a plot to injure him, or the like. The picture is familiar enough and at the pathologic level gives us at once the suggestion of the paranoiac with his hallucinations of hearing and his delusions of persecution.

The inferior organ, in this case the organ of hearing, can therefore be seen to be asocial in its tendencies, because it hangs on to infantile ways of pleasure-seeking, which should be abandoned as the individual grows to adulthood in favor of activities that minister more to the larger good. The individual, after all, can include only what is under central control, the dynamic or metabolic gradient, Child calls it[8] speaking of the physiologic individual.. A group of cells may establish their own independent gradient and so break off from the main body and

[7] White, W. A.: Hallucinations, Proc. Am. Med. Psychol. Assn., 1904.
[8] The Basis of Physiological Individuality in Organism, Science, April 14, 1916.

set up a government for themselves. This we recognize as one of the determiners of tumor formation. A similar independence at the psychologic level makes the individual, in the particular region involved, asocial. Asocial conduct may therefore found in organ inferiority.

Adler's theories are helpful in orienting the physician toward the larger problems which the patient presents, whether he approach it from the point of view of the internist or that of the psychologist. His theories are admirably calculated to help the internist to grasp the possibilities of organ inferiority as they may affect the psyche and to help the psychoanalyst to grasp the origin and meanings of the neurosis as he sees it at the psychological level, and perhaps to see more clearly on what his limitations are based. In any event the two groups of physicians, heretofore separated all too far, both in theory and practice, may find in Adler's views a common ground on which to meet.

PSYCHANALYSIS APPLIED

I have used illustrations which I have picked with care because I thought them simple and easily understandable. I might add a great many more of mistaken diagnosis, surgical procedures for mental states, etc. For example, we have a boy in the hospital now on whom a partial thyroidectomy was done for a hysterical globus, and I need only mention the delirium of ovariectomies less than a generation ago. All are familiar with such instances. Perhaps it is not appreciated, however, how insistent many patients are for operation, how they will argue most ingeniously for it, and seek surgeon after surgeon until one complies. Such patients are a positive menace, especially to the young surgeon who would like to operate anyway. The desire for operation may probably have many causes. I have in mind the case of a young man with a hysterical paralysis of the left leg.[4] The leg in its paralyzed state was only a nuisance and he wanted it amputated. Analysis showed the paralyzed leg to be a masturbation symbol. He wished to get rid of his masturbation by a species of sacrifice and penance. The paralysis disappeared as the result of a single psychanalytic talk. I recently saw a woman who had had three laparotomies, all more or less exploratory in character, because of pain, and so far as I could determine none of them showed any condition surgically removable. It was plain from my talk with her that the operations were engineered in order to maintain a childlike relation of dependence on the surgeon, of whom she was very fond.

The practice of medicine can no longer neglect the psyche; it must take into consideration the larger issues. A too refined medical specialism concentrates its attention on a particular organ and so is often blind to the meaning of the symptoms as they refer to the whole individual. The old medical specialism considered the organ out of its setting in the rest of the economy; the new specialism must consider the organ in its setting, and in this new specialism the psyche will have a considerable place.

Every once in a while one sees an ordinary illness, more especially some disease of the respiratory organs, "cold," bronchitis, or pneumonia, which investigation will indicate was intentionally acquired. Such illnesses are pretty apt to show on analysis that they are suicidal attempts. Such cases suggest that, when one finds a patient suffering from a disease due to exposure and the history shows a degree of carelessness out of all proportion to the patient's usual habits, it would be worth while to look deeper for motives. I am also reminded that some surgical injuries such as broken bones from falls and the like, may have a similar origin, either as an attempt at suicide or a form of penance. Time does not permit me to elaborate this motive. I can only say that it is universal. A good illustration of its present day forms is seen in the "conscience fund" of the United States Treasury, to which annually thousands of dollars are anonymously contributed. I need not speak of the importance of these facts when taken into consideration in connection with workmen's liability acts, accident insurance, sick benefit claims, health insurance, etc.

To acquire even a reasonable degree of proficiency in the technic of psychanalysis, as in any other department of medicine, requires careful study and much thought. There is no royal road. Work is the pass word. But if I counsel work it is not to avoid the issue and have psychanalysis shrouded in mysticism. The analytic results, often, perhaps usually, seem strange, sometimes grotesque. This is perhaps true of the last instances I cited, especially the young man with the paralyzed leg, and the examples of intentional surgical injuries. This is only because they are not formulated in familiar symbols. I have no doubt that many a medical student at his first clinic has looked on the lecturer, who could put his ear to the patient's chest for a minute and then talk for an hour on what he heard, as little else than a wizard, and has felt himself so incapable of ever being able to do likewise that he then and there has felt that after all he was afraid he could never

be a doctor. Devote as much time and attention to psychanalysis as this medical student had to devote to the study of percussion and auscultation and pathology and one will find oneself on quite as familiar ground.

In one wishes to enter the field of analysis, the first requisite is to be able to listen to what the patient says. It requires infinite patience and must be fortified by the conviction that everything psychic has a meaning just as truly as does everything physical. A physician would not let a patient sidetrack him from a physical symptom or explain it away. Similarly on the mental side. There must be a reason for everything, although the patient, often with great ingenuity, will slight the important, emphasize the unimportant, and in every way unconsciously try to mislead. Naturally, it requires some experience to deal with such behavior. The way to get the experience is to try it. No adequate attitude toward psychanalysis can be reached by reading alone; it is absolutely necessary to come into intimate personal contact with the problems in an actual, living patient. Before trying it, however, one should take a sufficient course of reading so as to have some idea of what one is trying to do. One will not have to try long before beginning to get a glimpse of what is going on behind the scenes, but it will be sometime before one can cope with any real difficulties. As soon as one begins consciously to try to learn something of a patient's psyche, it is surprising how much information may be obtained which will be of value.

Even if one is not disposed to do analytic work, let me suggest that, as psychanalysis is met in the literature from time to time, one's attitude toward it should be that of Leibnitz toward a new book. He said:

> It is characteristic of me to hold opposition as of little account, exposition as of much account, and when a new book comes into my hands I look for what I can learn from it, not for what I can criticize in it.

SEXUALITY

The reader may be wondering by this time why I have said almost nothing about sexuality. It is because I have not wanted to overemphasize it in presenting what I believed to be large, fundamental considerations. It certainly is not because I in any way minimize its importance, for I do not. Whether or not all pleasure found in sex, as I have suggested, is a matter of hypothesis. At any rate, the problem will be encountered among patients, and must be dealt with and

not run away from. With regard to this matter, I can do no better than quote Pastor Pfister of Zurich, who says:

> Psychanalysis is not only compatible with the highest ethical and religious demands but absolutely presupposes them. . . . The analysis has strengthened me in the conviction that the human being is in no way merely a sexual being of the highest order (which no psychanalyst has ever asserted) but that the varied mental wealth and noble characteristics which the idealistic has found in him, really belong to him. To be sure, I could not avoid the insight that the sexual life possesses a far higher significance in our mental household than the traditional psychology . . . is willing to admit.

It is objected that the psychanalytic procedure takes so much time that it is impractical. This complaint comes from the physicians, not from the patients. Perhaps it does take a long time and perhaps some way may be found to shorten it; but in the meantime we must make the best of it, and after all, that is no argument against the validity of the positions set forth. For my part, I doubt very much if the time can be materially shortened; the problem is too difficult, it means overcoming prejudice, instinct. To make the patients see themselves with intelligence is of necessity a long and tedious task, but no longer than the task of dealing with tuberculosis, although I grant you it does demand more time of the physician. But after all, what we are trying to do is to rebuild a personality. It is a problem in character reformation; and if we succeed in making a person over from a useless invalid into a useful citizen, who shall say that the time was not well spent? Remember, we must "give to the diamond its ages to grow."

DISCUSSION

JAMES R. ANGELL: Dr. White has just published a book, "The Mechanism of Character Formation," in which he has embodied many of the same views that he has set forth in his paper on "Psychanalysis and the Practice of Medicine." His book is the sanest and most lucid exposition of the conceptions of psychanalysts that I have met. I venture to read a few sentences from an article by the celebrated biologist, Iyves Delage:[1]

"In the event of a contagious malady making its appearance in any country it is the duty of the medical man who first has cognizance of the evil to raise a cry of alarm, so as to ensure the adoption without delay of the necessary prophylactic measures.

To sound this note of alarm is the object of this article.

This new affection, which threatens to invade France, had its birth in Austria, in Vienna, some twenty years ago. . . .

It is a malady without any apparent lesion of the central nervous system, a purely psychical affection; in a word, a psychosis. Its name, coined by the very persons who are its victims, is *Psychanalysis.*

[1] Journal of Mental Science, 1917, p. 60.

Psychanalysis, defined in the most general terms, is an affection in consequence of which the unfortunates who are attacked by it become incapable of accepting just for what they are the most insignificant gestures, the very simplest acts, the most banal words of persons with whom they have intercourse; in everything there must be discovered some profoundly hidden meaning. The detection of this pretended hidden meaning becomes for the patient a veritable obsession. . . .

Like all madmen, the psychanalyst lives in an imaginary world, which it is necessary for us to recognize in order to understand what goes on within him. . . .

Reader, what is your opinion?

I am of the opinion, you will answer, that there is no outrage on the most elementary common sense which psychanalysts are not prepared to perpetrate, in their efforts to square the very simplest and clearest facts with their preposterous notions."

It is not necessary to quote further to have one agree with me that the conservative statement which Dr. White has made is perhaps Freudianism at its best. I understand psychanalysis already to have reached a stage where it has begun to subdivide into cults and schools, so that it is no longer possible to say anything about it which shall be in any universal sense true. Freud himself has changed his views, has grown and developed. His disciples have likewise changed their views, and any attempt to evaluate the movement as though it consisted of a single body of well organized opinion is impracticable.

I understand by Freudianism partly a theory of the nature of the psychic organism and partly a system of therapeutics. On the therapeutic side I should hardly dare to express myself. I hazard a single comment. If one is to judge psychanalysis by its results, it is reasonable to bring it into context with other methods which, dealing also with the same specialized group of diseases, demand that they be judged by their results and not by their antecedent medical history. While the context is in some ways unfair and superficial, if one is really turning to results for a criterion, one may well ask whether Christian Science, mind cure, chiropractic, osteopathy, suggestion, hypnotism, psychic reeducation, and all the other things which have had more or less vogue in the treatment of nervous disorders, may not lay equal claim to success. Frankly, I do not pretend to know what the answer is—whether the successes of the Freudians are more readily gained, or are more permanent, or whether they cover a wider range of cases. But I am disposed to think that the question suggested has some propriety.

I have a few comments to make on the other side of the question, that is, Freudianism as a psychology, and more particularly its relation to other current psychologic beliefs.

I wish to speak first of a thing for which I think psychology greatly indebted to Freudianism. I believe Dr. White did not speak about dreams in his paper. But it is a statement of the most obvious fact to say that Freudianism has taught modern psychology that the dream is an absolutely significant and fundamental part of the psychic life of the individual, a thing which psychology prior to Freud had never in any frank, thoroughgoing way acknowledged. We had had all sorts of studies of dreams, but they were mostly on the descriptive level, and beyond affording a theory of the stimuli provoking the beginning of the dream, they had little to offer. They were, as a rule, wholly uninterested in the course of the dream or its interpretation. I am very far from wishing to imply that the Freudian type of interpretation is altogether acceptable, but there is a rapidly growing conviction that the analysis and interpretation of dreams presents a very real problem to our

psychology. Psychanalysis applied to dreams is at least as old as Pharaoh, for that eminent potentate had his dreams analyzed by a distinguished expert with disastrous results.

We are also under some obligation to Freudianism for again turning our notice to the far prehistoric past of man as bearing essentially on our conception of how the mind has come to be what it is. From one point of view it is, of course, true that this idea has been a commonplace ever since we learned to think in Spencerian and Darwinian terms. We have come to believe that you cannot understand the mind of living man today without recognizing that it has in it changes which are not only prehistoric but prehuman. Nevertheless, the Freudian has thrown a new light on the conception and has enabled us to take a more plastic and flexible view of the makeup of the individual than was heretofore the case. It is, therefore, no more than fair that we should acknowledge our indebtedness. We may also be allowed to voice a mild protest against the extravagant claims of certain Freudians as to their originality in this matter.

So far as concerns the antiquity of man's psychic past, our modern notion is not so different from that of the Freudian as might be supposed. It has been a familiar teaching of our textbooks on psychology for many years past that every person brings into the world with him a heritage of animal instincts, appetites, and tendencies, which in part reflect his descent from the race as such, and in part are due to peculiarities which may have become established in his own particular family stock. We have also come to recognize that there is mentally, as well as physically, an element of variation in every person which comes to the surface in impulsive traits—tastes, prejudices, wishes, and the like—which enjoy much the same kind of imperious claim over his attention as do those tendencies which derive more obviously from the common racial stem. Moreover, we have been for several generations thinking of the evolution of mental processes in the individual as taking place about systematized ideas and forms of reaction which at once suggest the Freudian complexes. These ideational systems grow up as centers of control in childhood and adolescence, and in maturity constitute the great groups of attitudes by which we maintain our social equilibrium. Underneath them all is always to be discerned the foundation of instinctive impulses to which we have referred. A serious disturbance in these impulses, either in the way of undue repression or in the way of exaggerated growth, is sure to be reflected in disturbances of the social attitudes and of the intellectual life.

The exploitation of wish fulfillment, or the 'libido' which the Freudians generally indulge, if taken in its earlier form as intrinsically synonymous with purely sexual impulses, has seemed to most psychologists grotesquely onesided. When enlarged to take in all the basic appetites of life, as in later Freudian writings appears to be the disposition, the doctrine either becomes substantially synonymous with the common views described, or it thins out into a formula so general as to be incapable of either proof or disproof. Modern psychology has given quite as central a place to emotion as has the Freudian, and in the movement headed by William James, the identification of emotional with instinctive behavior is substantially complete. The type of disturbances, therefore, which Freudians find originating from thwarted wish fulfillment, so far as these wishes are incorporated in emotional experiences, are easily assimilated to the conventional psychologic views, and, so far as concerns their theoretical implications are in no sense radically novel. Psychologists are quite ready to recognize the wide reverberation of the sexual impulses in the psychic life of the individual, but they have not for the most part been at all ready

to accept the earlier and more extravagant formulations of the Freudians tending to make this group of impulses absolutely predominant over all the others. Hunger and thirst, anger and fear, to mention no other items, all figure in primitive behavior in a fashion clearly distinguishable from purely sexual considerations, and any one may readily be implicated in disorders of the psychic life of the individual. To leave out these factors, or to slur them in the way in which Freudians have sometimes done, has seemed to psychologists to involve a distortion of the true conception of the psychic organism.

There is another matter on which Dr. White did not dwell, although it is admirably set forth in his book, that deserves consideration in this matter, that is, the Freudian notion of symbolism. No doubt you are aware how fundamental symbolism is to the Freudian conception of the dream structure. You also know how in the analysis of dreams, the psychanalyst distinguishes between the 'manifest content', the thing we common-sense persons are confronted by when we hear a dream described, or face one of our own, and the symbolic implication of the dream. We are told that only when we get the true symbolic clue can we understand what the dream really means. This assertion hangs together with the conception of the dream as a device for relieving repressions and permitting suppressed wishes to come into the mind in this veiled and roundabout fashion.

I cannot here enter with any thoroughness on this matter. Suffice it to say, that in a certain sense our conscious processes are all fundamentally symbolic. Language, the great medium of thought, is nothing other than an elaborate system of symbols. One does not need to turn to dream consciousness to verify the reality of the symbol as a feature of mental operations. What psychologists of the non-Freudian stripe have objected to has been the utterly weird and uncontrolled interpretation of dreams under the Freudian methods of analysis. The point is not that we are always in a position to prove the falsity of the alleged Freudian symbols, but that we are by no means bound to accept the wholly inconclusive evidence which the Freudian himself frequently offers for his own symbolic interpretation. Not even his ingenious search of the obscenities of primitive religious rites and practices has brought conviction to the rank and file of psychologic onlookers. Moreover, there is more than a little ground to suspect that just as in the Salpêtrière Charcot succeeded in unconsciously establishing a group of apparently real but actually artificial hypnotic states, so the Freudians are by their own procedure unconsciously generating a uniformity of symbolic interpretation which has little or no real convincing evidential basis.

Another interesting Freudian device, the censor, Dr. White also passed by in silence. The censor is the Freudian "god from the machine." On his behalf apparently is established the unbelievably elaborate system of symbols, by means of which he is coaxed into quiescence while these scapegraces pass out from the field of repression into the open pastures of the dream. Who he is, where he comes from, whether he is anything more than the accumulated moral habits of the individual—these and many other interesting questions about him are left unanswered. Meantime, he presents all the external characteristics of the medieval witch.

In conclusion, I should like to comment very briefly on one remark which Dr. White made in referring to the impossibility of securing a just impression of mental conditions under the ordinary procedure of the psychologic tests of the laboratory. It is quite true that our present forms of laboratory procedure are in some particulars ill adapted to the purposes of the alienist. But it would be wholly misleading to imply, as I think Dr. White perhaps unwittingly did,

that all laboratory forms of procedure lack practical value. Nobody who is familiar with the wide range of applications now being made in our laboratories and elsewhere of the principles of psychology to the practical problems of education, business, and industry, can for a moment accept any such implication. Moreover, it should not be forgotten that the most revolutionary contribution which has been made in recent years to the study of mental retardation and mental deficiency in children, is the contribution of a psychologist, Alfred Binet, and rests on distinctly psychological methods. I venture to believe, therefore, that while in general it may be true that the psychological laboratories are at present largely working on problems the solutions of which do not contribute immediately to the interests of the alienist, it is wholly beside the mark to deny to them very large contributions of a practical kind to modern enterprises of various sorts, and in general I think it may be fairly said that the actual procedure of the psychanalyst will be found to have been in considerable degree borrowed from the extant ideas and practices of our conventional psychology.

RALPH C. HAMILL: Concerning the rôle of symbols, perhaps a few incidents would clear the situation a bit. A young man came to me because of the physical symptom of tremor. Realizing what was back of this I rather minimized the symptom the first 2 or 3 times I saw him. After he had been coming for a couple of weeks I partially analyzed one of his dreams to let him see that he had not quite the ideals he consciously thought he had—that his conduct was not controlled by these ideals quite as consciously as he thought it was. The next day he came into my office very jauntily and said, "Well, I had a dream last night," and with a great deal of pleasure he told me this dream. He said he went into a barber shop, sat down in the chair and took great pleasure in telling the barber that he wanted a hair cut, but he did not want a shave, he did not want a massage, he did not want a shine, he did not want a shampoo, and he did not want his hair singed. I asked him what the barber looked like and he said he was over 6 feet tall, whereas his regular barber was a short man and a blond, and the dream barber was a brunette. It soon was apparent to him as to me that I was the barber, even as in olden days the barber was the surgeon. Also it was apparent that he wished me to stick to physical terms—continue to treat the tremor and cease to pry behind it, so I was forced to tell him that I might by hypnotism or suggestion be able to remove the tremor but I did not think that was the whole problem.

A little girl 11 years of age had been in the hospital for several days in an acutely maniacal condition. I listened to her delirium for 2 or 3 days and realized that going through all of it there was a current of ideas having to do with childbirth, so I spent an hour and a quarter with her telling her all about childbirth. Her father had been a lead worker and when she was 9 years old had been at home sick for a week, was taken away between 2 policemen in an ambulance to the county hospital, where he died 3 days later. Her mother went to work and the child brought herself up. She never interrupted me once as I told her this long story, whereas before I had never been able to hold her for a second. The next morning as soon as I opened her door she asked me this question: "Why were Adam and Eve thrown out of the garden of Eden?" I told this to the dean of the divinity school at the university and he said that the divines agree that the apple of knowledge represents sexual knowledge. It is difficult to think that this little gutter child could consciously elaborate this symbolism in 24 hours.

To emphasize the fact that she had not thought the thing up beforehand, another instance, in which the same mechanism appeared with the rapidity of a reflex, is that of a young man who after 2 or 3 weeks of analysis told me a dream which ended in a broken-down, tumble-down privy which he had slunk into get away from the threatening populace. A few weeks afterward he told me another dream ending up in a moving-picture house, a very respectable place, and spoke of his friends being around, in short an open frank situation. Then when he finished the recital he said, "I have had that dream before, the one that began on the bridge"—that was where the former dream began. I asked him why he called the 2 dreams one and the same when they were so different in their superficial characters. He said, "I don't know," then after a moment's pause I said, "What's in your mind now?" He said, "An apple comes into my mind." I asked him what name was in his mind, and he said, "Just as you asked me that the Bible came into my mind." He must have meant the apple of knowledge also. He had taken an entirely different viewpoint of his affairs in the 6 weeks intervening and when he was asked to explain the difference between these 2 dreams he immediately said, "An apple comes into my mind," this in a period of time in which it was impossible for him to formulate consciously such symbolism and yet it was the very thing that saved him a certain amount of face. He was a young man, 23 years old, and was not entirely willing to say that I had made that much difference to him, which he would have had to say if he had come out frankly and said he had taken such a different view of things. I find it difficult to think that anyone could deny the significance of this symbolism so corroborative of that of the little girl.

To go back to the little girl, I spoke of the fact that her father had been taken away from home by 2 policemen in a patrol after having been delirious for a few days, and that he died without her ever seeing him again. About 4 days after the experience when she asked me about the Garden of Eden, and during these 4 days she was perfectly quiet, the nurse met me outside of her door and told me that the patient had told her that she, the patient, and another girl had gone with two little boys into a vacant house and there had attempted intercourse. She spoke of this as "being bad." The nurse said, "Yes, you have been bad but you'll never be bad again."

The rest of the day following this speech of the nurse, the patient returned to her former maniacal condition. When I entered her room the next morning after the nurse had told me this experience, the patient greeted me with the question, "Will I ever see my father again?" I felt that in the question she thought not only of the fact that he was dead, but also of the fact that he had been bad, and that she had been bad. Consequently I told her that I did not know nor did anyone know for certain about life after death, but that I wanted her to understand that her father had not been bad. I might be criticized for assuming that she had any such thoughts in her mind, but the results have justified my assumption, for after telling her that society approved of intercourse between married people, and that it was a necessary function in order that children might be born, she quieted down and has been normal at least so far as her mother, her various teachers, or I have been able to determine. This last conversation was a little over a year ago.

Dr. White spoke of the habit of taking things to replace others. Dr. William Healy asked me to work with a kleptomaniac. He sent me a young girl of about 18. She told me about the things she had stolen, told me about her early childhood, and then suddenly said, "When my little sister

was 15 she had a baby and I would rather do anything in the world than that." I worked with her for 2 weeks. There was never anything sexual in her story; it was all of the type of the bad boy in school who is the hero of the room. At last she told me a dream to the effect that she was dragging a box across the street and she could not get it across. When I asked her to tell me about this dream, she could not or would not tell me a thing. This failure of associations had been going on for 2 weeks and I felt that things were in her mind that should be brought out, so I said to her, "We are just wasting time this way and unless you can tell me the things that come to your mind, we can't go on; if you will talk freely tomorrow we will go on, but if you cannot be frank with me you need not come." She came the next day and then told me that she had a dream the night before. I asked her what it was and she told me the following: "I went into an ice-cream parlor and a man came in and sat at the next table and commenced to edge his chair against mine. I went out of a door but instead of going on to a street it led me into a little room at the back and the man followed me in and threw his arms around me and kissed me." To make the story short, the kleptomania came at the end of a 3 days' struggle to prevent herself from masturbating. She was then 15. At the end of that struggle she stole from her patroness, the person who was giving her the one chance in life; she stole something which she could not possibly use, a brooch which she could not possibly wear as long as she remained near that woman, and she left it on her dressing table in the room next to the woman's from whom she stole it. The stealing was not useful, but she had said in referring to her sister, "I would rather do anything in the world than that," and so instead of the greater crime she committed the lesser. She had to give way, but chose the less reprehensible.

If we did not follow up these symbols in the analysis it would be a tremendous waste of the evidence that is offered to us. We are criticized for using them and told that they may mean anything. That may be true, but on the other hand they may lead us to a much better understanding of our patients. If so, they should be followed up just as any other line of clinical investigation is to be followed.

HUGH T. PATRICK: That the majority of practitioners, I may even say of the most highly educated practitioners, neglect the psychic factor in sickness is to me only too apparent. In the investigation of an obscure case, there are thousands of physicians who will carefully analyze the urine, make blood counts and blood cultures, give repeated barium meals and make numerous Roentgen-ray pictures, examine the spinal fluid, have a Wassermann done, do a von Pirquet and a few other tests, but so far as the really vital life of the patient is concerned content themselves with a few superficial questions about overwork and worry. In other words, they assiduously cultivate an intimate acquaintance with the patient's organs and fluids, but overlook the man himself.

What is the man himself? It is his total character with all his passions, desires, fears, beliefs; his susceptibilities and his lacunae of feeling; his attitude on duty, religion and love, on money, health, heaven and hell; this is simply the born animal plus the resultant of his reactions to all of the influences which have been brought to bear on him. The neuroses, big and little, serious and amusing are certain reactions which we call abnormal because they are unusual. How are we to understand a given one and consequently handle it wisely unless we find out how it came about?

The question whether or not psychanalysis is the best way to ferret out the origin of, and also the best way to treat the trouble has not yet been answered

to every one's satisfaction. The excellence of any therapeutic procedure can neither be affirmed, denied, nor estimated on a priori grounds. Its relative value can be ascertained only by intelligent comparison of its results with the results of other methods. Consequently the therapeutic value of psychanalysis is not to be determined by psychologic investigations however interesting or startling the revelations of such investigations may be. Even very clear reasoning on conflicts, repression, and displacement, shown by psychanalysis to exist, does not establish its therapeutic value. On the other hand what looks like clean logic to the effect that psychanalysis is futile and probably harmful does not prove its therapeutic uselessness.

Furthermore, a man who has not used it cannot know whether it is better or worse than the methods he has been using. But, conversely, the psychanalyst who is not familiar with the older methods has no means of comparing the two and hence no grounds for vaunting the high value of his own procedure.

This brings me to my personal opinion, if I am entitled to an opinion, being neither a psychologist nor a psychanalyst, but just an old-style practitioner.

1. The first step in psychanalysis is simply intelligent, painstaking, and detailed history-taking. This, I am convinced, pays. And in many cases, after getting the patient's confidence, it pays to ask leading and intimate questions.

2. There can be no doubt that experiences which the patient has forgotten may have been of great importance in the genesis of a psychoneurosis. Perhaps as frequently something the patient has not forgotten is quite overlooked because it has no obvious connection with the nervous disorder. The patient says nothing about it and the doctor does not dig it out. A simple instance is the following:

A happily married woman complained of general nervousness, poor sleep, and several minor disturbances all of which proved to be part of or to take rise in a somewhat indefinite but sufficiently intense agoraphobia. She hated to go outside the house, even with someone. To go to market was a task seldom accomplished because it caused general tremor, great weakness, palpitation, and apprehension. She never went out to see her friends, though friendly and fond of companionship; she even dreaded to have her friends call on her. The ordinary causes of agoraphobia seemed to be absent. There was no fear of sudden loss of consciousness, of heart disease, of apoplexy, etc. There was no fear of accident, of assault, or other untoward happening. In short, an hour's interview was fruitless and she was turned over to my associate, Dr. Pollock, with the following result:

At the first sitting there was an hour of explanation, reassurance, and instruction as to what was wanted; at the second sitting she related the story of her life from childhood on without anything of importance being revealed, and at the third sitting, further details in history were given, but no helpful facts. The patient was instructed to remember and recount her dreams. At the fourth sitting she related an apparently insignificant dream, but showed some irritation or disgust because in the dream she seemed to be fond of a rather casual acquaintance or friend. A little investigation then uncovered the fact that in the dream this person really represented another. This led to the discovery of a series of decidedly scandalous events during the childhood and youth of the patient which were obviously the cause of distressing selfconsciousness. This in turn grew into the agoraphobia. Now, this woman had not at all forgotten these early experiences but it never occurred to her that they could have anything to do with her present trouble. And in spite of her instruction and her promise to tell everything, it required a Freudian dream

interpretation to elicit the thing we were after. When she saw the genesis of her trouble and its reasonableness, the agoraphobia disappeared.

3. What the psychanalysts call the 'libido', which I think might be called the longing for the joy of life, is a real thing. "Be good and you'll be happy" is an old admonition. For many of us "be happy and you'll be good" is quite as applicable. Could we at one stroke make the whole world happy, we should have a much better and healthier world. Each one of us has an inherent hunger for something more than food. Many of us are so constituted that if this inward craving be not satisfied, we react in some way which we call functional nervous disease. Of course the practical moral is to uncover such unsatisfied longing or aching emptiness and then fill it with an adequate activity.

4. The statements of patients are to be discredited for 3 reasons: First, they may have forgotten essential things; second, they suppress events or symptoms they wish to conceal; third, they may not be fully conscious of present states of mind. For instance, a patient will honestly deny fear, jealousy, unsatisfied desire of some sort, when such state is not only present but very intensely so. It is for the physician to discover these unknown states of emotion.

5. One final, simple point, which I believe is sometimes overlooked by psychanalysts as well as others, is that by means of psychanalysis the old conflict and repression which gave rise to the substitution—the neurosis—are laid bare. The patient sees how his symptoms came about, sees the process and understands it as his doctor does, is satisfied, and hence is cured. But is he cured because the true explanation has been given him? Not necessarily so at all. He is cured because he believes or feels that he has the true explanation. Psychanalysis or ordinary understanding may present the patient with the true genesis of his disorder, but if the explanation does not fully and completely satisfy him he is not cured. On the other hand a quack or a Christian Science healer may give him some spurious logic or an activity based on such spurious logic, which does appeal to him, which does satisfy him, and he is cured.

THE RELATIVE VALUES OF PUBLIC HEALTH PROCEDURES

CHARLES V. CHAPIN
PROVIDENCE, R. I.
April 24, 1917

What constitute the msot effective lines of effort is the most vital question confronting every public health administrator. Money is the measure of most effort, and appropriations are limited. In what way shall the appropriation for the health department be expended so as to save the most lives and prevent the most sickness? Are our municipal health departments making the best apportionment of their funds? Are health officials devoting the most effort to that which will best conserve the health of the people? If any city is doing this, it has a model health department.

Certainly many cities are not doing it. It is hard to break away from tradition. Most persons think largely in terms of the past. Institutions are of slower growth than knowledge. It is a pity that they cannot be kept in closer alinement. Though it would be sad, indeed, to chase every pseudoscientific will-o'-the-wisp that happens across our path, it is even worse to cling tenaciously to the dead ashes of discredited theories.

Modern municipal health work began at a time when it was believed that municipal house cleaning was the chief, if not the sole, legitimate field of official sanitary activity. Sanitary science has progressed by leaps and bounds. Sanitary administration has been a laggard. It would be most interesting to see what sort of health department would be organized if all tradition could be ignored. Given an appropriation of, say, 75 cents per capita, how would a commission of modern scientifically trained and experienced public health men organize a health department, if they were permitted to discard tradition and take cognizance only of the present day findings of sanitary science? Our health departments are not made in this way. They are the result of growth. One function after another has been grafted on the original duty of nuisance abatement, but the growth has not been well balanced. Health work does not extend according to any well thought out plan, but one duty after another is added, now by

this person and now by that. Sometimes the health department is expanded at the instance of a group of earnest reformers having much sympathy for human ills, but little versed in medical and sanitary science. Sometimes a city councilman, getting his knowledge from the syndicated science of his Sunday paper, assumes to tell how the health department should be run. Again, it may be the new health officer himself who, in order to justify the political overturn of his office, seeks to reorganize the health work of his city after a few hours' study of some passing book on 'sanitation.' Rare, indeed, is it that competent advisers are called in to plan a health department so as to utilize most effectively the best scientific knowledge of how to preserve the health of the city, and it is more rare still for the politician to permit such a plan to be put in practice.

RELATIVE VALUES

Even those health officers who have given the subject much careful consideration do not feel sure of the relative values of different lines of health work, and it was to help clarify my own ideas as well as to assist in what I believe will be a helpful discussion that the attempt was made not long since to assign numerical values to the various functions of a municipal health department. It is said that no science can progress unless accurate measurements are made of the things dealt with. In accordance with this idea, it seemed desirable to indicate by figures the value of garbage disposal and of the diagnostic laboratory, of plumbing inspection and of baby nurses, and thereby learn how to apportion the funds and energies of the department.

In attempting to make such a distribution we must constantly bear in mind that the appropriation cannot be exceeded. A certain percentage of the funds may be set aside for contagious disease work, a certain percentage for school inspection, a certain percentage for vital statistics, and so on, but they must all add up to 100% exactly. If we should yield to the behests of every enthusiast, championing his hobby, the sum might be 200 or 300%, resulting in a most uncomfortable deficit. So, too, time and strength are limited, as well as money. No man can work more than 60 minutes in an hour. To assign values to functions, so that time and money may be apportioned accordingly, is the purpose of the schedule here presented.

Unfortunately sanitary science is as yet far from an exact science. Its measurements are crude. For many things we have no measure-

ments, but only estimates or guesses. It is desirable, however, to correlate even our guesses.

The table of values is intended to indicate the relative importance which should be attached the functions which are commonly performed by a health department in any average northern city at the present time. The apportionment must vary somewhat according to location, stage of sanitary development, character of the population, etc. In the South, where there are much hookworm, typhoid fever, and other diseases spread through fecal infection, excreta disposal must receive special attention. Where Anopheles and Stegomyia

TABLE 1
Relative Values of Health Work

	Vital statistics	60
	Education	80
	Laboratory	50
	Control of nostrums	50
	Care of sick poor	50
Food	Adulteration	0
	Sanitation	10
Milk	Adulteration	3
	Sanitation	17
Nuisances	Privy sanitation	60
	Housing	20
	Plumbing	10
	Nuisances	10
	Refuse removal	0
	Fly and mosquito control	10
Infant mortality	Nurses	80
	Supervision of midwives	10
	Babies' boarding houses	5
	Milk stations	5
	Consultations	20
	Prenatal clinics	10
	School inspection	80
Contagious diseases	Home isolation	100
	Hospitalization	50
	Immunization	50
	Venereal diseases	20
Tuberculosis	Nurses	60
	Dispensaries	40
	Hospitalization	40
		1,000

abound, antimosquito measures come to the forefront. If the rodents of a city are plague infected, or likely to become so, the rats must be fought. A well sewered city can appropriate money for other lines of work which in less fortunate places must be devoted to the never ending task of privy sanitation. Every city must plan its health work to suit local conditions, but there will probably be only minor variations from the generalized type.

Experience is the best teacher. Methods which have been successful in the past must be followed in the future. There has been a marked decrease in the death rate during recent years, but it has not

been all along the line. The bulk of the improvement has been confined to a few diseases. Thus in Providence, in 60 years, there has been a decrease in the annual number of deaths amounting to about 600 per 100,000 living, and confined practically to typhoid fever, smallpox, scarlet fever, diphtheria, tuberculosis, diarrheal diseases, and other diseases of infants.

It is not for a moment claimed that all of this reduction is due to conscious effort on the part of the community, though I believe that a good part of it is. Thus there has been a reduction in the death rate from pulmonary tuberculosis of about 240; but as it began long before any efforts were made for the control of the disease, we must believe that much of the reduction is due to unknown causes. As the decrease

TABLE 2

MEANS OF SAVING LIFE

Typhoid fever	10 by direct control
Typhoid fever	50 by privy control
Scarlet fever	60 by direct control
Diphtheria	20 by direct control
Diphtheria	30 by free antitoxin
Diarrhea, over 1 year	15 by privy control
Tuberculosis, pulmonary	65 by direct control
Tuberculosis, other	15 by direct control
Infant mortality	70 by nurses, etc.
Infant mortality	10 by milk control
Total	345

TABLE 3

RELATIVE VALUES OF COMMUNITY ACTIVITIES

Direct control of contagious diseases	26
Direct control of tuberculosis	23
Antitoxin	9
Control of privies	18
Prevention of infant mortality	21
Control of milk	3
Total	100

in recent years has been fairly rapid, and has followed well thought out methods of control, it is perhaps not unfair to assume, as I have done, that a drop of 65 deaths per 100,000 may be attributed to present day methods of combating this disease. On the other hand, probably the whole of the decrease in typhoid fever is due to municipal effort. It seems fairly conservative to claim, as a result of community health work, at least half of the decrease in acute communicable disease above referred to which has occurred in Providence. The figures in Table 2 appear reasonable as a statement of the deaths prevented by official control and also of the chief means by which the lives were saved.

By putting the facts in a different form, it appears that community activities have been effective in saving these 345 lives in the ratios given in Table 3.

These are old and tried lines of public health work, and must hold the largest place in apportioning the activities of a municipal health department.

There are many other activities, the value of which cannot be measured at all, or only in the crudest sort of way. Some of these we know are of great importance, while others are still in the experimental stage and, though we cannot tell just how much they are worth, must be given a fair trial. In our table of values they can be given only an arbitrary rating.

BASIC FUNCTIONS

Of fundamental importance is the collection and tabulation of vital statistics. It is only by this means that evils can be located and remedies found. It is as difficult to put a health value on vital statistics as it is for a merchant to put a money value on his ledgers; but as the merchant decides to expend on his bookkeeping enough to get correct results, so the municipality must spend enough on its vital statistics to make them tell the truth. Perhaps this is fairly indicated by the relative values here assigned.

The education of the public in matters pertaining to health is another basic function, which, until recently, has been much neglected and is now often injudiciously performed. The leaders of thought and action in each community must be made familiar with the successes of modern sanitary science and the means by which they are obtained. To teach the politicians is another story; but if the leaders think the public health worth while, the politicians will, too. To reach the great masses of the people is more difficult still, particularly the foreign peoples in our cities. The literature which is read and digested by the thoughtful farmers and merchants of the country falls on stony ground in the foreign quarters of our cities. The movie may help somewhat, but the personal influence of the schoolteacher, the nurse, and the social visitor have thus far seemed to accomplish most. An arbitrary value must be assigned to this function also. One is tempted to write the figure large, but the knowledge that the sum of our values cannot exceed 1000 reminds that we must not rob Peter to pay Paul.

The great leavening force in modern health work has been the diagnostic laboratory, the handmaid of epidemiology, as it has been called. To control disease, either by prevention or by cure, we must first find it. This the laboratory helps us to do. The remarkable apparent decrease in the case fatality of typhoid fever during the last

20 years or so has been due almost entirely to better diagnosis by the help of laboratory methods, so that many cases are now discovered and properly cared for which formerly would have been unrecognized. Not only has the laboratory taught us to recognize mild infections of typhoid, diphtheria, and syphilis where they were not before suspected, but it has taught us by this experience to look for the atypical in other diseases, in which the laboratory can as yet give no direct help, as in scarlet fever and smallpox. Doubtless the laboratory in all our larger cities is continually saving lives, but there is no way of measuring this any more than there is for the merchant, to return to our former simile, to place a money value on his yardstick and his scales, yet he could not do business without them. The diagnostic laboratory is worth all that it costs, and perhaps its value is not unfairly indicated in the schedule.

The care of the sick poor outside of the hospital is not usually considered a health function. Yet there are a number of cities in this country in which it is performed by the health department. In 1 or 2 it is treated seriously, for there are some who consider it primarily a health rather than a charity problem. Sickness and poverty are closely related, and the poor, from both necessity and indifference, neglect sickness. To secure for them prompt and efficient care should save many lives and discover much early infection. About one quarter of the cases seen by the physicians to the poor in Providence are acute infections, and a considerable percentage of the others are such as usually come within the cognizance of a health department. This function must be performed efficiently. Slipshod methods, superficial examination, and perfunctory prescribing are not much better than nostrum taking, pure and simple. As the medical care of the sick poor is in a chaotic, transitional, and experimental stage, a moderate value has been assigned to it. It is not impossible, however, that in the not distant future the municipality will furnish or direct, by adequately paid physicians, medical service, and not only for the poor, but also for a considerable part of the population. This function should be performed by the health department so as to be properly coordinated with the other activities of that department.

THE NOSTRUM EVIL

Closely connected with the last subject is the elimination, or restriction, of the nostrum evil. If it is proposed to get rid of the

latter, good medical service must be supplied in its place. The one common excuse of the poor for patronizing medicines is that they cannot afford to pay a physician. Conversely, I have confidence that a conscientious efficient medical service for the poor will do more than anything else to wean them from nostrums. This dual purpose is frankly acknowledged by those active in the restriction of venereal disease. An active campaign is waged against nostrums and the advertisers, and at the same time efficient clinics are organized. This combination, needed for the proper treatment of venereal disease, is probably needed just as much for all other diseases. The campaign against nostrums, which has been waged so heroically by the American Medical Association, has also been entered into by some state departments of health. A few cities, too, have taken active measures to the same end. While energetic action is not always feasible, probably nearly every municipal health department could do something, and many of them could do a great deal to eliminate this sickness-prolonging and death-dealing evil. An experimental value must be assigned to this function also.

SANITATION AND FOOD CONTROL

According to popular notion, the principal functions of a city health department are sanitation and food control. When a health department is mentioned, most people think first of an inspector of nuisances. To them municipal housecleaning is the chief duty of the 'board of health.' Improved housing, plumbing inspection, garbage disposal, street cleaning, 'clean-up week' and antifly campaigns are even now, by our most intelligent people, considered the chief business of the health officer. If the latter does not put his whole heart and soul into such concerns, but neglects them that he may apply himself to the cure of syphilis, the provision of nurses for tuberculosis, the establishment of infant welfare stations, the prevention of blindness in babies, or the improvement of the eyesight of schoolchildren, he may find himself in marked disfavor.

Some municipal sanitation is of great and direct value in the prevention of disease. The improper disposal of human excreta is the chief cause of typhoid fever, cholera, the infectious diarrheas and dysenteries, and hookworm infection. Where there is no system of excreta disposal, as in some of the rural portions of our country, and where the summer is long, this subject may well, at first, have a large

part of the health department's attention. In a thoroughly sewered northern city, with few privies, and decent housing, excreta disposal requires comparatively little attention. The inspection of plumbing is important from a health standpoint only so far as it relates to excreta disposal. We need good plumbing as we need good chimneys, and both are essentially parts of building inspection. So also, nuisance inspection, except as it relates to excreta disposal, is concerned far more with esthetics than it is with health. The odors of decay which strike terror to a careful housewife are really not half so annoying as the exhaust from an automobile, or the fumes from the oil on the macadam road. Neither will cause real sickness; nor are papers and tin cans in the vacant lot a source of disease. All these things shock our sense of decency, and they ought not to be; but why burden the health officer with the arduous task of remedying them? The police should do all that, but they usually decline.

In a considerable portion of our cities, the health department is charged with the removal of garbage and often of other kinds of refuse. This has only the most indirect and tenuous connection with health, though no one questions for an instant that it should be done and done promptly and well; but it is essentially a function of the department of public works.

Concerning the relation of housing to health, except for the grosser forms of bad housing, we know very little. That better houses encourage higher standards of living is probably true; that higher standards of living mean higher wages is not improbable; that the sickness rate decreases as wages advance is doubtless true, and that the restriction of crowding and an abundance of light and air facilitate personal as well as household cleanliness and so check the spread of infection is quite likely to be the case. The beneficial effects of good housing on health are largely indirect. Much besides housing affects health indirectly. A good trolley system, industries that pay high wages, a clean city government, an effective school department, must all react favorably on health. If the health officer went into every scheme for civic betterment, his labors at refrom would leave him no time to look after syphilis and tuberculosis, diphtheria, and ophthalmia. He had best concentrate his fire where it will do the most good and where he is, or should be, most competent to direct the attack.

Much has been written about the fly and his wicked work. In some places he is more dangerous than in others. Where the summer

is long and privies are many and there is much initial infection, this insect may be a considerable menace. It is difficult to see how it can be so in a well sewered northern city. Last year Boston had the lowest typhoid death rate of any American city, 3.5 per 100,000 living; but Boston has not carried on any effective antifly campaign. Providence has its full quota of flies, and is otherwise not a very clean city; yet our typhoid death rate has fallen from 69.4 to 5.1 by means of pure water, the abolition of privies, and the following up of cases. The diarrheal death rate has fallen from 252 to 106. If we could get rid of all our privies and pasteurize all our milk, our typhoid rate might vie with Boston without our touching a fly. To exterminate flies is costly. If the people wish to pay for abating this nuisance, well and good. As a citizen I would vote for it; but if as a health officer I had $10,000, I would not swat the fly but would open a venereal clinic, or hire some nurses for the supervision of tuberculosis.

In nonmalarial regions the mosquito, like the fly, is a nuisance, but not a menace to health; the mosquito should be held down to the lowest limit, and most citizens are willing to pay the cost. It may even be that the special appropriation would best be spent by the health department, as biologic knowledge is more likely to be found there than elsewhere in the city government; but it should not be counted as an expenditure for health. Of course, in a malarial region mosquito control is a most important health measure which has received altogether too little attention.

Another time-honored and popular means of promoting the public health is control of the food supply. This control naturally is divided into the prevention of adulteration and the promotion of cleanliness. Though there is much lurid literature on the dangers of impure food, as a general thing adulterants are as likely to be healthful as unhealthful. Adulteration, with rare exception, is an economic and not a health problem. There is almost as much nonsense written about ptomain poisoning as there is about adulteration. 'Ptomain poisoning' is the popular name for disorders arising from bacterial changes in food. Of such we really know little except that they are not nearly so common as is believed, and that the routine inspection and condemnation of cabbages and corned beef, as practiced by our city health officials, probably has no effect in restricting the somewhat rare occurrence of such poisonings.

That food is not rarely infected with human secreta and excreta

by those who handle it, and thus becomes a real factor of importance in the transmission of disease is certain. It is worth while to try to check this, though the efficiency of some of the popular 'sanitation' of markets and restaurants may be questioned. The elimination of infected food handlers also gives some promise, but its true value is yet to be determined. The small value here assigned may arouse protest, but who will argue that the laboratory is not 5 times as important, or baby nurses 8 times as important, or the direct control of contagious diseases 10 times as important as is food sanitation ?

Milk should be considered apart from other foods. It is certainly of great importance in infant feeding, though the close dependence of infant mortality on the character of the milk supply has probably been considerably exaggerated. Many cities have markedly reduced the infant death rate without greatly improving the cleanliness of the milk. Doubtless the most effective way to eliminate the danger from milk is to require the pasteurization of all milk, or at least all except a limited amount of a certain high standard, for infant feeding. The watering of milk is an adulteration which does effect health, for a veriable composition sadly interfers with exact methods of infant feeding, and likewise increases the danger of infection.

OTHER ACTIVITIES

Firmly believing, as I do, that all the medical activities of the municipality should center around the health department, I naturally consider the medical inspection of schools a proper function of this department. As a matter of fact, it is somewhat of a cooperative undertaking, and neither the school department nor the health department can properly carry it on without the free and generous assistance of the other. Tact and forebearance are needed on both sides to carry on this important work, no matter which department has it in charge. The vast majority of both teachers and medical men connected with school inspection are satisfied of its great value, but it touches school life in so many ways that a statistical demonstration of its benefits is by no means easy. Without such statistical data, it is difficult to assign a definite value to this function. The one given in the table is only tentative, and may well be subject to revision.

Another and quite new activity is the campaign against venereal disease. That this is of great importance no one denies; as to methods, however, we are still in the experimental stage. We do not as yet

know what results can be obtained, though the future is promising. It does not seem unreasonable, as is here indicated to devote 2% of the energies of the health department to this object.

ACTIVITIES WITH DEMONSTRABLE RESULTS

The sum of the values thus far assigned is 400. That is, to the activities of the health department which we have reason to believe are worth while, but the utility of which we cannot very well measure are allotted four tenths of the energy of the department. There are thus left six tenths, or 600 units, on our scale, to be divided among those activities, the worth of which can be measured, with some degree of approximation, in terms of deaths prevented. These allotments are made in accordance with my judgment as indicated in the first portion of the paper.

While it is difficult to estimate the real worth of school inspection, that other branch of child welfare work known as the prevention of infant mortality has a value which is demonstrated perhaps more decisively and accurately than in any other form of preventive medicine. In practically every instance in which a community has undertaken to save the lives of its babies, it has been successful. The chief means has been the education of the mother. Wherever that has been successfully accomplished, the infant death rate has fallen. Taking the actual reduction of 80 per 100,000 of the population in Providence, and assuming that 70 of this is due to specific effort made for that purpose, we should, according to our plan, allot a value of 126 to baby welfare work; but as this is such a promising field I have ventured to steal a little from the control of contagious diseases, and as a final estimate, 130 has been allotted. How this shall be divided among the different kinds of infant welfare work will depend somewhat on individual judgment, and may soon change as a result of wider experience. Perhaps the division here indicated may receive a fair degree of approval.

The direct control of the communicable diseases by isolation and immunization was an important duty of the health department even in that period of the last century when the dominance of the filth theory of disease had relegated it to a subordinate place. According to the best evidence at hand, there has been a marked decrease in the amount of several important contagious diseases against which fairly active measures have been taken for a considerable series of years.

In cities in which the records have been kept for from 50 to 70 years, and active restrictive measures have been carried on for some time, typhoid fever, scarlet fever, diphtheria, and smallpox have shown a phenomenal decrease. That this decrease is due in large part to the measures which have been taken I believe is true. Even the decreased virulence, which is responsible for part of this decrease, I have elsewhere suggested is probably partly due to the selective restriction of the more virulent, and hence more easily recognizable strains, by our methods of isolation. Among methods of control, isolation in the home is probably the most important. To secure this, special medical inspectors or trained epidemiologists have the chief place, but visiting nurses are becoming more and more useful. It will perhaps be a surprise to some that the hospitalization of acute contagious diseases is not given a higher value, as it has often been alleged that complete hospitalization would stamp out disease. This, however, it fails to do because of the unrecognized sources of infection. Hospitals are needed and needed badly for those patients who are so situated that home isolation is impossible, or who are in need of hospital care. So far as the spread of disease is concerned, the majority of patients can be taken care of fairly well at home. The great expense of the hospital is justified fully as much on humanitarian as on sanitary grounds. Its value as a health measure is perhaps fairly indicated by the rating here given.

Vaccines and curative serums are most valuable in the control of infectious diseases. Experience has shown that the use of these agents depends in great part on the initiative of the city or state. In one way or another, by furnishing at low cost, or perhaps without charge, and often by administration, the sanitary authority can succeed in popularizing methods of prevention or cure which otherwise would be little used.

A modern campaign against tuberculosis makes use of many means, and is often correlated with various private agencies. Outside of diagnosis and general education, perhaps the most important municipal activities are nursing, dispensary service, and hospitalization. There may be a difference of opinion about the relative value of these, but the figures given perhaps fairly represent present day views. Certainly hospitalization, which a few years ago was considered of first importance, has been relegated to a secondary place.

It may be asked why the protection of the water supply does not

find a place in this discussion. It might perhaps do so, but it is more properly a function of the state department of health to guard water supplies, though some of the larger cities have resources sufficient for independent action. It is rare that a local health officer has any management in water works. It is his important duty to show by his morbidity statistics whether or not the water is above suspicion. So, too, industrial hygiene is omitted because it also is more often controlled by state officials. A number of newer activities, such as the campaign against cancer, or the degenerative diseases, or the prevention of mental disease, are omitted because it was deemed unwise to let this discussion get too far afield, and better to deal with actualities rather than with possibilities.

THE AIM OF COMMUNITY HEALTH WORK

It is particularly urged that the values here assigned are not final. Even among the most careful students of sanitary science there would doubtless be considerable difference of opinion. Some of these differences would disappear after free discussion. It is partly the purpose of this attempt at valuation to bring out such discussion. Minor changes might be made, but no discussion will ever demonstrate that plumbing inspection is worth more than baby nurses, or that swatting the fly is as effective as abolishing the privy vault. The purpose of the paper is not to enter a special plea for the exact values here presented, but to show the need for perspective in planning health undertakings. If relative values had been carefully considered, the ill balanced health department which was recently brought to my attention would never have grown up. In a city of 100,000, home isolation receives only such time as the health officer can spare from his executive duties, while money is available for 6 nuisance inspectors. There is a fumigator, but no diagnostic laboratory; 3 food inspectors, but no baby nurses; and several plumbing inspectors, but no welfare stations or prenatal work, and no Wassermann tests or venereal clinics.

The figures given in the schedule are intended to indicate, though ever so roughly, the real health-conserving value of certain common functions of municipal health departments. It is not intended that either money or time should be apportioned in exactly these ratios. The cost of an adequate hospital for the care of advanced cases of tuberculosis would be many times greater than a good system of dis-

pensaries and follow up nurses. With limited funds, the dispensary and nurse comprise the most economical and effective undertaking.

If the health work of the future is to be successful we must remember first that the old, ill founded idea that health work is to be centered on the environment has been displaced by the modern one, well supported by the data of science, that it is concerned directly with men and women. We would all like to live in spotless, flyless towns. Streets should be clean, yards tidy, houses neat, every garbage can covered, the cellar whitewashed, never a tin can on a vacant lot, every market white tiled, all bread wrapped in paper, and every laundry immaculate. This is for what we have campaigns and health weeks and for which appropriations can be obtained; but it would have little effect on the death rate. Mothers would continue to feed their babies with pickles and cookies; scarlet fever would spread; diphtheria would claim its toll; people would forget to be vaccinated; schoolboys would strain their eyes at their work; careless syphilitics would become paretics; ill treated poliomyelitis would make cripples; the man with 'grip' would swallow tonics and cough medicines until he gave up work and his infant child died of tuberculous meningitis, and lifelong blindness would result from ophthalmia.

Municipal housecleaning will not cure these evils, but education, isolation, and good medical care will. Community health work must have a broader outlook. It must do more than cleanse and isolate. It must make use of the best medical knowledge, not by stealing or begging it, but by paying for it, to prevent and cure disease. Many activities must be coordinated. Much has been done. There is more to do. Until there are unlimited money and unlimited talent available, let us earnestly study to do that which pays best.

DISCUSSION

HEMAN SPALDING: I regret I did not know Dr. Chapin was to present this table of relative values. Had I known, I could have made a survey of conditions in Chicago to compare with his table.

In his table, I do not believe hospitalization and education have their rightful value. I believe hospitalization should be valuated 100 at least. In Chicago, if we can hospitalize every case of infectious disease, such diseases can very nearly be kept out of the city. I would not think of trying to control smallpox in a city like this without a hospital for isolation of every case. Under present conditions, that is the only way we can control the spread of this disease. Home isolation which is valued at 100 in this table, is nothing less than numerous small hospitals located at various places in the city. This is more expensive and more dangerous to the public than a single isolation hospital. Home isolation may be practiced in towns and small cities, but not in a large city.

I would not think of trying to control an epidemic of any infectious disease without a hospital for isolation. This is one thing I insist on. I know the evidence adduced against hospitalization, but the failure to get favorable results is not because of hospitalization, but because of inefficient hospitalization. I should certainly valuate hospitalization above home isolation.

Education should be valued higher than 80 in the scale. For many years I have thought that education should hold the foremost place in our health work. Recently I have changed my views somewhat about the method of education. Talking in churches, lecturing in halls and before social clubs to grown-ups who have their fixed ideas as to how to live given to them by their mothers perhaps does little good. Most of them soon forget what is told them, and go on in the way they were early taught. But there is a method that will bring results, and if I could have my way, I would put it into operation. I would have places—health centers—where people can get authoritative information on health matters. There should be capable teachers who command the confidence of the community, so people will believe what is told them. As a rule, people would rather be right than wrong, and in the main they will be right if the truth is presented in an authoritative way. Information that is known to be true only should be given out, and then people will soon learn to believe and follow such advice.

Chicago has 45 police stations, which cost a lot of money just for handling criminals. Why not build health centers where the well can learn how to keep well? I would establish a social health center for every 25,000-100,000 inhabitants, according to the needs of those in the various districts. I would have a municipal building for each of these social centers. These buildings should contain an audience-room where talks could be given and moving pictures exhibited; also health posters and other educational exhibits should be displayed and literature on health matter given out. Little mothers' club meetings could be held in this room also. There should be room for infant welfare work, where mothers could bring their babies to a doctor for instructions how to feed and keep the baby well. From this room, nurses could make a house-to-house canvass for all babies and find and give instruction to prospective mothers. I would have a free dispensary, equipped to correct defects found in children, at school or at home, whose parents are too poor to employ a physician. I would have a dental dispensary for helping the needy poor. There should be a laboratory to do the necessary work in the district. Free baths could be located in the basement.

From such a center, sanitary health officers and food inspectors could work. Such a center should have an all-time health officer and an adequate number of health officers and nurses to do the work of the district. These health centers can be directed and receive assignments from a central office, and make daily reports of work done.

With health officers and nurses in the field, little mothers' clubs in daily session, educational work in the assembly room every evening, and the other activities mentioned for the municipal social health center, we could get to the people who most need information.

I would also establish children's clubs in these centers, as we now have in a few of the public schools.

I would establish a chair of hygiene in every public school and conduct little mothers' clubs in all the schools.

If this plan could be put in operation, many of those first cases of contagion would not occur, and the effort to prevent the secondary case would be saved.

JOHN H. LONG: I should like to ask Dr. Chapin about the position given to the question of food adulteration on his chart. I am not sure that I understood him correctly, but I thought he said that while this question is of importance, it is not of sufficient importance to take the time of a health department. I understood him to intimate that entirely too much time is given to the discussion of the dangers of food adulteration, and that is the point of view I have maintained for many years. We have been at times hysterical over the food adulteration danger, and have worried far more than the situation warrants. The adulteration of food is largely a commercial proposition, consisting mainly in the substitution of a cheaper for a dearer article. This is a matter for the police, rather than the board of health. What is called adulteration in some cases is often a protection, and on this statement, as made by Dr. Chapin, I am in full agreement. The addition of formaldehyd or hypochlorite to milk may, as the lesser of two possible evils, be at times justified, and the same may be said of the use of other so-called preservatives under certain conditions.

CHARLES V. CHAPIN: It does not seem to me that the adulteration of food has much effect on health. The addition of adulterants is rather a matter affecting economics. As far as health is concerned, they are sometimes of distinct advantage, as when water is put into whiskey or ground cocoanut shells into cayenne pepper. The cleanliness of food is of much more importance. I trust that I did not suggest that the control of the milk supply as regards both adulteration and cleanliness is not important. It is important, though it has been somewhat exaggerated. We ought, if possible, to have milk free from adulteration and with a low bacterial count.

I sympathize with Dr. Spalding in his criticism in regard to education. I too, should like to assign a greater value to education, but do not see exactly what functions should be robbed for this purpose, unless perhaps it is nuisance control and plumbing inspection.

Concerning the hospitalization of contagious diseases, I think its value has, by many, been overrated. We must have hospitals and they are very important, but not all important. Hospitalization will not stamp out disease. In a number of English cities over 90% of the cases of scarlet fever have been hospitalized for many years and most of the other cases have been well isolated at home, yet scarlet fever is more prevalent than in the United States. If I were in Dr. Spalding's place, I should earnestly demand more hospital space for Chicago, for this city, at present, has not nearly enough beds for the purpose of handling contagious diseases. Perhaps half of the cases of scarlet fever and diphtheria in a city should go to a hospital; the remainder can be well isolated at home. In Providence, it has been found that these diseases spread from one family to another in the same house, after the warning sign has been placed, in less than 2% of the cases and this could be considerably reduced by more effective inspection and nursing, which would be much cheaper than hospitalization.

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of the

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MODERN METHODS IN WAR FROM A MEDICAL STANDPOINT

SURGEON-GENERAL J. T. FOTHERINGHAM, C.M.G.

ACTING DIRECTOR-GENERAL MEDICAL SERVICES, CANADA

November 2, 1917

I do not appear before you as anything else than a physician who has for many years given to the question of the military defenses of his country the attention which these problems demanded. I do not come as the professional soldier, of course, but I do come as one who has had a very deep interest in the problems that confronted the military officials for many years. I do not come to say anything particularly new or to rouse any discussion of the broader medical problems of this war. For one reason — I have had service only in the collecting zone, that is, in the area in which the armies are actually fighting. I have had no direct experience other than a theoretical one outside of that zone, either in the line of evacuation or in the zone of distribution from the front. Nor do I bring you any professional details, either medical or surgical. When there is time later on to collect statistics and make proper deductions, these will be done. Of that sort of work I have no word for you tonight. I should, however, like to bring to you from the front and from the Empire to which I belong, from that part in particular from which I come, a word of good cheer.

We in Canada in particular have felt, so far as those to the south of us were concerned, that we were always ready to go to the length of speaking of you as our cousins, but we certainly now prefer to speak of you as our brothers. We have felt that our position in the Empire was peculiar in this that we were destined by our geographic location to be for the Empire and for you the channel of transmission from the older civilization of Europe to this country of those things which would do not only the older motherland a service, but would do you in receiving a service and would do us in transmitting also a service. The greatest satisfaction to the English so far accrued from the entrance of the American people into this war is our conviction that Anglo-Saxon ideas are definitely and finally in the saddle in this country, and, whatever differences may have existed in the opinions

of those outside, your country has been converted, not *de jure* but *de facto,* and the United States is again in the Anglo-Saxon federation of the world as a result of this war. As a result of this war, there is, of course, no thought of anything in the British Empire in the nature of an alliance. The feeling on the part of our people in the British Empire is that cooperation, such as we now have, will not again be lightly interfered with, and those relations will be more fruitful of good throughout the world, as well as fruitful of good to the Empire and yourselves, than if they were made legally closer, while the feeling of cordiality and good will, which now exists, we feel is not again to be broken. That is one of the results of your entry into the war which appeals to us very strongly. We also feel that the war as it is developing cannot be finished without you. My own feeling is that the war will be ended in two or three years with France still in the war, Great Britain still carrying on, and yourselves still going strong, the latter both from a financial and military point of view.

I ask you to bear with me while I try to make you see the war as I have seen it myself. In order to do that, I have brought with me a somewhat formidable array of documents, which consist of my own war diary for all the time I was there and the official appendices I have made to it. Perhaps you will pardon me if I begin by saying that my duties were those of the medical officer which we, in our service, call Assistant Director of the Medical Service of an Infantry Division. All the administrative services of an army are in charge of Directors and Directors-general. The Director of the Medical Service is the medical officer in charge of the army. There are five British armies in France, averaging from 400,000 to 500,000 men in each. The army is made up, as you know, of corps. The corps has a deputy director at the head of the medical services. The corps is made up of divisions, usually three, sometimes two and sometimes four. The medical head of the division is known as the Assistant Director of Medical Services. They have a director in each army, a deputy director in each corps and an assistant director in each division. There are about 20,000 men of all ranks in a division. Twelve thousand of those are infantry in 12 battalions of 1,000 each, in 3 brigades, each of 4 battalions. The remainder, about 8,000, include about 3,000 artillery, counting in the ammunition column. The remaining 5,000 include the army service corps and engineers and the army medical corps, military police and other details. Of the latter, about 850 are under the command of the Assistant Director of Medical Service, in the

form of three field ambulances (or A. D. M. S., as we call him for short), just the same as the four battalions of an infantry brigade are under the hand of the brigadier. The military duties devolving on the brigadier in regard to his infantrymen devolve, also, on the A. D. M. S. as regards his ambulances, and, of course, this gives one a very great deal more military experience than it does professional. In front of the field ambulances, one has a regimental organization which consists, as you know, of a medical officer, with first a water duty detail of four privates and a corporal, whose sole duty it is to take charge of the water for the battalion. Then there is a sanitary section with the battalion, a corporal and eight men for sanitary duties, so the medical officer has under his hand three little bands — his water duty detail of five, the sanitary section of eight, and the sixteen stretcher bearers, four per company, combatants trained in first aid, with as many more as possible for the making up of casualties among the sixteen.

I shall give you a brief history of the Second Division to show you just what service we had. We went from Canada in April, 1915. By the end of September, we were settled in Belgium, from the south of England, first in the salient at Ypres, and were there for eleven weary months. They then moved us south to the Somme, where we had two periods of duty of 11 and 13 days each, to which I will come later. They then moved us up north a bit to the north of the Souchez River and in front of the Lorette ridge. Then shortly after they moved us down to the Vimy ridge, just north of Arras. After having taken part in all the preparations for the taking of the Vimy ridge, against my will I was sent home to Canada, so I was not present at the fighting which resulted in the taking of the ridge, though the ground is thoroughly familiar.

I have referred previously to the three areas into which the seat of war is laid out by the medical authorities for their practical purposes. The first is the collecting zone, in which occurs the actual fighting; second, the zone of evacuation, which contains the lines of transmission over which the wounded have to be sent; third, the zone of distribution, in which they rest until they are recovered or otherwise. As I indicated, my duties lay entirely in the forward area in the collecting zone. I think that I can best give you some idea of the type of the activities of the collecting zone if I begin by reading some reports sent in to me by a couple of regimental medical officers to show what sort of work they had to do. The one is dated Jan. 17, 1916,

and it is from a very efficient medical officer in charge of a battalion during the time they made a well-prepared raid.

January 17, 1916.

From M. O., 21st Battn.
To A. D. M. S., 2nd Can. Div.

Operations of January 17, 1916.

Sir:—I have the honor to make the following report on operations carried out by 21st Battalion on this date. Regimental aid post was at M 9 C1½ 2-in the railway cutting.

Approach to R. A. P. was via Porthcawl Road and Lemberg Trench. This is an excellent approach from the part of the line on which operations were carried out.

Wounded were cleared from R. A. P. via railway cutting to Grenay Bridge. This also proved to be an excellent road, though several shells of small caliber fell in the railway cutting. These caused no casualties. They were intended, I think, for the brigade machine guns which were on both sides of the cutting.

Prisoners were made use of for clearing wounded to field ambulances.

Casualties are as follows: Officers—Capt. Donald McKenzie Goudy (slightly wounded); O. R.—killed, 4; wounded, 61; missing, 7.

Company officers have nothing but praise for the good work done by the stretcher-bearers. My own assistants did excellent work, the corporal and two men having been recommended for recognition of services.

R. A. P. was taken over at 7 a. m. Except for isolated cases, wounded were cleared by 9:45 a. m. R. A. P. was vacated at 12 noon.

I have the honor to be, Sir, your obedient servant,

(Signed) A. E. Cooke, Captain, C. A. M. C.

The approach to which he refers is an excellent approach for the part of the line on which operations were carried out. The wounded were carried from the regimental aid post by the railway track, a long cutting. This proved to be an excellent route of transportation. We had several experiences of the nature mentioned in the report, where shells had gone through ambulance wagons or cars, killing some of the wounded. I must admit that a great deal of what is said about the shelling of medical establishments is incorrect. It is impossible to distinguish the hospitals and aid posts, and I am sure that very often shells intended for some other places strike the aid posts or cars containing the wounded, just as this medical officer states.

Here is another report. This one is from Capt. W. H. McGill, C. A. M. C., one of the best medical officers I ever knew or wish to know. He was with the Thirty-First Alberta Battalion, and when I left he was one of the surviving four original commissioned officers of the battalion.

C. O. 31st (Alberta) Battalion.

Herewith short report of the evacuation of casualties sustained by 31st battalion in operations from September 24 to 28, inclusive, please.

While battalion was halted, resting along Sunken Road, north of Contalmaison, on afternoon of Sept. 25th, enemy commenced a very severe bombardment about 1 p. m., and battalion, in the space of a few minutes, sustained 28 casualties; 3 killed and 25 wounded (1 officer and 24 other ranks). The officer (Lieut. H. P. Morgan) was wounded in thigh by a fragment of shell.

The battalion sustained some further casualties in taking up position in trenches north of Courcelette on night of September 25 and 26, but none of them passed through my hands.

In company with my two orderlies, I arrived in Courcelette at 8:30 p. m., September 26 and established my R. A. P. in a deep dugout, known as the "Tunnel," located at R. 30. a. 6.5. I notified the A. D. S., No. 4 Field Ambulance to this effect. No casualties came in during first night. During next afternoon, September 26, Capt. H. Hawley was attended and passed on to A. D. S. After attack in afternoon of September 26, the wounded arrived in a constant stream, and, at times, we were badly congested, as our accommodation for lying cases was limited. The enemy shelled the surroundings of our R. A. P. very vigorously and almost constantly, so that I was naturally very anxious when it was necessary to leave stretcher cases lying in the short trench at door of dugout. During the height of the afternoon rush, I was very reluctantly compelled to send a number of cases straight on to the collecting post of A. D. S., without re-dressing, as I considered it unwise to have a collection of stretcher cases in such a dangerous area. We utilized, as far as possible, the slightly wounded as stretcher bearers from R. A. P. to collecting post of field ambulance.

We were unable to clear all our wounded before dark, and had to keep nine seriously wounded in the dugout over night, the terrific enemy bombardment of village made it too dangerous for carrying parties for a time. The following morning, the C. A. M. C. bearer squads helped us to clear our wounded and continued to do so during progress of action.

During the second night, September 27 and 28, four lying cases were kept at R. A. P. over night. These were cleared early next morning by C. A. M. C. squads.

There was little trouble in keeping R. A. P. cleared on September 28, but a number of cases arrived at dusk which we kept over night, as shelling was again quite severe. These were evacuated this morning by field ambulance bearers. I turned the R. A. P. over to Captain Argue, M. O. of 26th Battalion, and left at 7 a. m. this morning, September 29.

During our tour of duty in Courcelette R. A. P. we passed the following cases through: three officers, Capt. H. Sawley, 31st Battalion, Lieut. J. N. Mee, 31st Battalion, Lieut. G. H. Scott, 31st Battalion; 100 N. C. officers and men—of these, 32 were stretcher cases and the balance walking. The 3 officers, and 76 O. R. belonged to the 31st Battalion. The remaining cases represented seven different units.

The regimental stretcher bearers, as usual, did remarkably fine work under most difficult conditions. Lance-corporal T. Bright and Pte. T. Willis, my orderlies, did splendidly, and I wish, in a special report, to bring to your notice the especially fine work of the latter.

(Signed) W. H. McGILL, Captain, C. A. M. C.

Medical Officer, 31st Alberta Bn., C. E. F., C. A. M. C.

I only read these to give you some idea of the point of view of the regimental officers at the front.

Now, as I have not prepared a formal address, I shall simply pass from one topic to another as they occur in my war diary.

The next topic I would like to take up I would introduce by reading you a very excellent report of a gas attack by one of the medical officers. About the gas I may say, of course, as all the world knows, the Germans introduced it, though it was contrary to all international agreements. I felt, at one time, that our cause being good, we should not consent to use gas, or otherwise fight the devil with fire. I feel now there is no reason why we should not use it—ten times as strong and ten times as much of it. This is not a time to be squeamish as to international relations. There is no harm in our violating part of our agreement since the Germans have violated all of theirs. We do know that the new gas does more damage than anything they had. The drift-gas from cylinders opened when the wind suited has been given up, or almost so. The gas shell, capable of being fired at long range, was improved on by us at least to this extent, that drums of concentrated gas in liquid form are fired at comparatively short range from gas projectors, or modified trench mortars. These gas shells came into wide use last spring. This has been extremely effective. The gas, I believe, is a modified hydrocyanic, or something of that sort. It does not kill, as the other gas did, by suffocation or strangulation. It kills almost instantly. The latest German gas is known as "mustard gas." I had a letter from an A. D. M. S. the other day, in which he told me they had completely mastered that. Our people send out tubes or flasks to the front lines in which they collect the gas when it is going, and bring it in for analysis. They have thus secured knowledge of all enemy gases, definitely, almost as soon as they are used.

I may, perhaps, be allowed to read, as I have jotted down here some points of interest, from a paper of mine in the *British Medical Journal* of Oct. 13, 1917:

A summary of the activities of the C. A. M. C. may be made under three headings:

1. Preventive medicine;
2. Clinical progress in medicine and surgery;
3. Laboratory and research work.

In regard to preventive medicine, the two outstanding features of the situation are: (1) preventive inoculation, and (2) sanitary control in the field.

Preventive Inoculation.—That, of course, applies to those under the voluntary system, as we simply refused those who did not signify their willingness to be vaccinated. Now with compulsory service we are faced by a different situation. Just a short time ago, the Privy Council passed an order under the War Measures Act by which not only is inoculation compulsory, but making it a military crime to decline it. I incidentally included in that paragraph a requirement that any one required by superior authority must submit to blood examination and the Wassermann test.

Quite a number of cases of tetanus originate in trench foot. It was found necessary a year ago to order that all cases of trench foot must be inoculated against tetanus. The dose has been as a rule 1,500 units. The serum has been to a large extent, but not exclusively, obtained from the Canadian Red Cross Society, and is that manufactured in the laboratories of the University of Toronto through the thoughtful provision of a wealthy benefactor there. The regular source of supply through the advanced depots of medical stores has also been drawn on. Comparisons and results are not available as yet, but there is no doubt in the minds of all in a position to judge that, as a preventive measure, the procedure is proved to be indispensable.

The same remark holds true, if possible more positively, with regard to antityphoid inoculation. When regard is had to the practical absence of true typhoid and to the extraordinarily low incidence of the other diseases of the enteric group on the one hand, and to the universal contamination of the water supply by the colon group on the other, one may truly say that a new chapter may now be written in the history of military medicine, and that the world at large owes to Sir William Leishman and the R. A. M. C. a debt which it can never repay; and it should not be forgotten that the millions of men now in the war zone and far from their accustomed strains of enteric infection represent, without inoculation, virgin soil for the ravages of the disease.

Smallpox has been practically nonexistent among the Canadian troops, as each man signs in his attestation papers a contract to undergo vaccination, which is universal.

Dysentery has occurred in a slight, sporadic form, but not as either epidemic or endemic. Such cases, even though only suspected, are sent to a special hospital in each army direct from the field ambulance admitting, by motor ambulance convoy car.

Sanitary Control in the Field.—The two important parts of this many-sided problem are water control and disposal of waste. The organization necessary is briefly as follows:

1. Battalion and unit sanitary sections, specially detailed and trained by unit medical officers and employed under their direction. Responsibility rests with each O. C. for his own lines, the M. O. acting as adviser.

2. Divisional sanitary section under a specially qualified medical officer, who is also divisional sanitary officer, under command of A. D. M. S. of division, reporting to him, and employing the other ranks of his unit as inspectors over the whole area occupied by the division with reference to water supply, disposal of waste, and conservancy arrangements of every sort.

The opinion has been steadily growing that for the semi-siege type of warfare so far prevailing on the Western front, too frequent moves of these divisional sanitary sections detract seriously from their usefulness, and that they should, within limits, be made more permanently responsible for the areas with which they have become familiar, after the manner in which town majors and camp commandants are employed.

With respect to the protection of the water supply, in addition to the supervision maintained by the divisional sanitary sections, which is good, the Canadian corps has in action a water patrol. This patrol places a second check on the chlorination of water.

Water patrols, covering a Canadian corps area, are in charge of an officer under the "Q" branch. A survey is made, maps prepared, and information collected. The corps area is then subdivided into patrol sections, each section being patrolled by one N. C. O. and five men (permanent base). The duties of these patrols are as follows:

(*a*) To see that rivers, streams, ponds, wells, and springs are not polluted.

(*b*) To see that no washing and no watering of horses are done at any but authorized points.

(*c*) To see that no material connected with the corps water system is destroyed or renewed without corps or divisional orders.

(*d*) To visit daily each of the water tanks, stand-pipes, etc., where water carts are filled, collecting the daily report from the "divisional control" in charge.

Divisions are responsible that all orders regarding chlorination and "water details" are carried out and also all instructions, such as those mentioned in Paragraph b. Any unit not complying with instructions regarding water supply is reported by the water patrols to the water patrol officer, but this does not relieve divisions from their responsibility for seeing that all instructions are carried out. When a unit is reported to the water patrol officer a report is forwarded to the division concerned. Should the same unit be reported a second time, a report is forwarded to corps headquarters. Men belonging to, or attached to, the divisional sanitary sections are detailed as "water controls" by the O. C. sanitary sections for all authorized supplies in the divisional area. These water controls keep a "daily tank report" in triplicate, which sets forth the conditions of carts drawing water, conditions of chlorid of lime, etc. A copy of these reports is forwarded daily to the divisional sanitary officer, one copy to water patrol officer, and one copy is retained as record by the water control. The divisional sanitary officer is responsible that the necessary steps are taken to prevent a recurrence. The O. C. water patrols summarize these daily tank reports once a week; a copy of this is sent to the D. D. M. S. A record is thus kept.

Other matters pertaining to water supply are also reported to the D. D. M. S., and thus the medical services work in conjunction with the other branches to maintain as adequate and good a supply of drinking water as possible.

The incidence of water-borne diseases in the Canadian corps has been low, and it may be said has only occasioned anxiety when conditions were such as to interfere, or prevent, the maintenance of those measures which have been indicated above.

Of course, nothing would prevent the men from drinking what they thought was good spring water rather than chlorinated water. I have not a doubt that, were it not for the universal practice of inoculation, we would have a great deal more enteric disease than we had. As it was, we had practically none.

Reference should be made to the very important topic of baths and laundries. In most British divisions, it is understood that these establishments are under the control and administration of the A. D. M. S. for the "A. and Q." branch of the staff. In the Canadian divisions the practice has been to relieve the medical service of this responsibility and to place in charge a capable business man who is an officer seconded from his unit to the staff of the division. This has given excellent results and would seem to be less wasteful of the special

training of the medical officers, though close co-operation always exists between the A. D. M. S. and the officer in charge of baths and laundries through the A. A. and Q. M. G. The Foden-Thresh disinfector, for instance, which is on charge to the sanitary section and under the control of the A. D. M. S., is kept in operation at the divisional baths, where the men exchange their soiled clothing for fresh. Ordnance by arrangement makes issue of socks and underwear through the baths officer.

With regard to clinical medicine and surgery, I am not going to inflict that on you, because I do not feel that I have anything worth while to contribute. I do want to say a word about the dental service in the army. In Canada the dental service is arranged as distinct from the medical, though in France the dental officers were employed under orders of the medical service. Members of the dental corps have been of great assistance to us. There is a dental laboratory where dental appliances are made, 3 or 4 miles away from the front, instead of having to send down to the base laboratory. The loss of military time for dental causes has been reduced to a minimum. Apart from dental work, these men take the same duty as medical officers. We employed the dental officer to do dressings when hard pushed, which he can do just as efficiently as the medical officers in the ordinary run of cases at the dressing stations. For instance, in our Somme engagement, during the time I was in charge of the evacuation I had my twelve horse ambulances in front with six horses each—that was seventy-two horses with 450 bearers. I placed a dental officer in charge to supervise and maintain efficient work by this forward party and he did perfectly well. I wish the two services were united. In France, under the British Expeditionary Force, the dental service was placed completely under the medical, as it was realized that only one channel should be permitted by which, for reasons connected with his health, a man can evade military duty. That has been quite satisfactory both to the dental and medical officers.

Just a word perhaps, if you will allow me, in regard to trench foot. Of course, Belgium is known as the place of origin of this new and very serious cause of military disability. Long before Caesar's time they fought in Belgium and Germanic Gallia, but we find no mention of trench foot in Caesar's writings. The first thing that occurs to me is that Caesar was a wise man. After his summer's campaign, Caesar put his troops into winter quarters and made straight for Rome where he had politics to see to, and where the sun shone bright and he never saw a case of trench foot. Even in Marlborough's time we do not hear of trench foot. The reason was that there was no skilled medical care, though Marlborough was the first great general to pay serious attention to the medical needs of his troops. In essence, trench foot is a case of severe chilblain complicated by infection. It is not frostbite. Apart from the predisposing causes, such as overexertion, lack of warm meals, and other things that keep men below par, the three actual causes are the three conditions of cold, plus wet, plus infection. The temperature that produces trench foot most generally is from 3(to 40 F. Long exposure to wet is an absolute essential. Unless th

epithelium is broken down, you will not get trench foot, because infection cannot easily penetrate the skin while dry. These three actual causes are of course effective on at least three structural elements of the foot, namely, epithelium; the corium with its vascular and connective tissue elements, and, lastly, the nerve endings. The vascular disturbance due to prolonged moderate low temperature causes capillary stasis with a moderate amount of edema and with change of color, first pallor then redness. The combined effect of wet plus infection and disturbed nutrition from defective blood supply is to produce sloughing more or less severe. The nerve symptoms are those of neuritis, hyperesthetic and anesthetic areas being found in combination, the latter the later stage. Great tenderness frequently exists, so that the patient prefers to keep the foot bare and exposed from beneath the blanket. They may be classified, according to severity, into three groups: (a) mild, usually recovering in about a week, but leaving a decided tendency to relapse; (b) moderate, requiring at least a month, and (c) severe, requiring six months or more to heal, and frequently involving more or less amputation, according to the degree to which the bones had been exposed by sloughing. It was, during the first year of the war, a very serious cause of disability. For instance, in the first winter, 1914-1915, up in the Ypres salient a British brigade was forced to make a hurried march of 17 miles. To get in about dusk the brigade had to start without time for rest or a hot meal. They were about 4,000 strong when they went into the trenches after that march. They were in there for 18 hours or more, up to the knees in mud and water, and when they came out 2,300 of them were useless for the rest of the winter from trench foot. They might as well have been shelled out of existence so far as further military usefulness was concerned. That was in the first winter of the war. The prevention of trench foot is not primarily a matter for the medical officer — it is a matter of discipline. The troops should have at least one hot meal a day, no matter whether they are in the front trenches or not. The general officer of my division made the occurrence of trench foot a matter of discipline. The commanding officers of the battalion, company and section in which trench foot occurred was simply told he would get no leave for some months. The effect was so great that one could not help being impressed by the decline in the number of cases. I had prepared my weekly report on trench foot one day for the general officer commanding the division and had just signed it, when the

divisional ordnance officer came in. I passed it over to him and said, "Look at that." He said, "That is queer, look at my list." He had just prepared a list of the waste of gas helmets, and the very battalion which was the worst in my list held the same place in his list, a clear evidence of the bearing that discipline has on the incidence of trench foot.

Not to delay longer on that point, I have taken the trouble to bring these helmets with me, because I thought they would interest you. These are steel helmets. There are three of them in which the men were killed and two or three in which the men's lives were saved. There is a legend attached to each one. If you will kindly pass them around, you can read them. While that is being done I can tell you some little things about them. Here is the point of entrance. Here is the attempted point of exit. The man was killed by the bullet inside as the legend will show. There is not the shadow of doubt that these helmets have been the greatest life savers possible. They do not look pretty. They look very awkward. They are cold in winter and they are beastly hot in summer. Here is a very interesting one. You will see that that dent in the side was produced by a rapidly falling bullet at close range. It did not enter, but went off without injuring the man. This helmet was one in which an officer was killed by a piece of shell. It did not deflect, but dented the helmet and fractured his temporo-parietal bone in such a way that he died in a half hour. I find in my diary a note on steel helmets which I sent to the deputy director of medical services of the corps soon after the issue of the helmets.

D. D. M. S. Canadian Army Corps.

Steel Helmets.

It may be of interest that I should report observations on the results seen in three cases of men struck in the head by rifle bullets while wearing steel helmets issued to the troops. They present the following points in common:

1. Practical absence of ill effect to the men by concussion, although knocked down in each case. Only trivial scalp wounds were incurred without any loss of consciousness or serious disturbance, each of them walking immediately without assistance, some hundreds of yards, to the regimental aid posts.

2. In each case the helmet was penetrated and in two an aperture of exit exists in a line different from that indicated by the opening of entrance, showing deflection so that the bullet traveled round in the space between the helmet and the scalp, inflicting a trivial scalp wound, in no case reaching the bone.

3. The three factors in this very desirable result appear to be: (a) resiliency of the steel; (b) space of about three-fourths inch between the steel and the skull, and (c) the buffer provided by the soft rubber pieces fitted to the lower edge of the lining.

4. The number of cases so far studied is insufficient to justify too sweeping conclusions, but we have not yet had a serious head wound in the case of any one whose helmet has been struck although it is safe to conclude that the helmet saved the life of its wearer in each of these three cases.

(Signed) H. M. Jacques, Lieut.-Col.
For Colonel, A. D. M. S., 2nd Canadian Division.

Sir Anthony Bowlby, consulting surgeon to the 1st and 2nd armies, told us not very long after these helmets came into general use, that the records already showed that they had reduced the mortality from head wounds by 50 per cent. This is interesting, particularly when it is borne in mind that in trench warfare the exposure of the head alone is much more frequent relatively than in open fighting.

SICK WASTAGE

Just a word or two about sick wastage. I have a report on the sick for 2 weeks ending Feb. 26, 1916, and March 5, 1916, two consecutive weeks. There were 4 corps in the army, each corps, the 2nd, 5th and 14th British and the Canadian corps, consisting of 3 divisions, so there were roughly 60,000 in each corps. The 2nd Canadian division during those two weeks stood at the top of the list bracketed first with a British division with a wastage of only 35 per thousand for the first week and 28 per thousand for the second. Although we did not maintain that by any means all winter, we did come out at the end of the winter with as good an average as any corps in the army. I find that on that occasion I sent out the following notice to the medical officers of the division:

The A. D. M. S. 2nd Canadian Division has much pleasure in expressing to all ranks of the medical service in the division the appreciation of the G. O. C. division of the very satisfactory showing above set forth. This high standard has been in part attained by the care and effort of the medical officers, and can be maintained only by steady devotion to our special duties in the service of His Majesty the King and of the Empire.

The next month, April 28, to show you how such matters fluctuate, I had to send out, I find, the following instruction:

April 28, 1916.

O. C.'s Field Ambulances, M. O.'s i/c Units.

Sick Wastage.—During April the curve for sick wastage has gone up, as it always does, with the curve for killed and wounded. From holding the best general average in the 2nd Army, the division has dropped to the foot of the list, and is now 14th in order. The General Officer commanding the division

desires that this be rectified as early as possible, and therefore, while fully recognizing the efficiency of the medical service and not reflecting unfavorably on us, requests that the fullest co-operation of M. O.'s i/c Units be given to the combatant officers in all matters that can conduce to the health of the troops. Points suggested are:

1. Securing all possible rest for the men while not in trenches or on necessary duty.

2. Controlling the cooking and feeding of the men, and particularly seeing that hot food is available at night for working parties and during tour in trenches.

3. Attention to regular use of bathing facilities.

4. Doing everything possible to have water of proper quality available both from water carts when in rest and at points of storage in trenches and strong points. All water-bottles, tanks, water carts, rum jars and other containers must be kept clean by disinfection at least once weekly with strongly over chlorinated water.

5. All other points bearing on the men's health, such as drinking in estaminets, care of feet, attention to sanitation of lines and areas, both in trenches, strong points, billets and camps, and particularly water discipline as the dry season comes on, will be daily insisted on by the medical officer in his contact with all ranks.

Inoculation.—Small remaining details not yet re-inoculated against enteric and paratyphoid will be completed by arrangements with unit authorities, but not so as to interfere with tactical needs—even during periods of rest.

Officers commanding units—The M. O. will arrange to go over this memorandum with his O. C. at the latter's convenience.

(Signed) J. T. FOTHERINGHAM, Colonel,
A. D. M. S., 2nd Canadian Division.

The working parties referred to in P. 2 are the bane of the soldier's life. The men would rather be holding the front line really than in brigade or divisional rest, because from the latter they are constantly called up, from 500-800 men per battalion at a time, for working parties. This usually means a tramp into the front line, from 3-5 miles, to arrive there as soon as the fall of night makes it possible to do so without being seen, struggling all night in the darkness with sand bags and wire and trench digging, etc., frequently under bursts of machine gun or shrapnel fire when shown up by the star shells or flares, then tramping back in the morning wet, tired, and dirty.

Perhaps in the same connection another record from my diary may interest you. It is a record of the sick and wounded of the Canadian corps from June 1-10, 1916. Not to burden you with details, the summary is as follows:

Admissions to the 12 field ambulances for the 10 days named totaled....	5,873
Evacuations totaled	4,729
The difference between these two figures..........................	1,144

This means that the ambulances were able to save to the divisions that number of men for early return to duty. Of course, they were mainly overtired or slightly wounded cases, but if the field ambulances of the division were not doing their work well these men would either through neglect have broken down finally, or been at the time evacuated to the base and lost to the divisions unnecessarily. While it is true that the hospital phase of field ambulance work is very limited, it is also true that intelligent use of these medical units means much more than simply collecting of the wounded, first aid, and clearing of the area.

I should like to mention at this juncture the whole hearted cooperation with which we were always met by both the British and the Canadian Red Cross Society. Whenever we moved we took over on receipt from the unit which we were relieving all the material in excess of mobilization tables which had been provided for the various rest stations, etc., in the area by Red Cross people. You understand, of course, that mobilization tables specify most rigidly the amount of transport and the load of each vehicle, and that accumulations, however necessary, of material in excess of the mobilization table must be left behind when a move is ordered.

SANITATION

You can quite understand that keeping clean trenches and dug-outs and underground sleeping quarters in the front line trenches present problems different to those in camps or barracks. As illustrating the precautions necessary I may read you an instruction to all medical officers in charge of units sent out on July 8, 1916. As an example of the difficulty referred to, incineration at the front is impossible. Everything must be buried, as the least sign of smoke usually brings instant shell or machine gun fire or a rifle grenade or two. Even the cooking has to be done in the front line by charcoal, or alcohol, or over a petrol lamp.

July 8, 1916.

To All M. O.'s i/c Units.

Sanitary Conditions.

1. *Visits of Inspection.*—Each M. O. i/c Unit will during his unit's tour of duty in front, support or reserve trenches, and strong points, carry out a daily personal inspection and will see the whole of the lines occupied by his unit at least once every 48 hours. He will be accompanied by an officer of the company and the sanitary detail of the company whose lines he is inspecting, and will

severely check any laxness observed in the discharge of their duty by his sanitary section in supervising and reporting to him.

He will make a daily report to his O. C. of conditions as he finds them, and of his recommendations for their improvement, and will send every third day to the A. D. M. S. a duplicate copy of his reports to the O. C. Unit, stating the extent to which his recommendations have been carried out.

2. *Points to Be Noted.*—(a) Latrines: It will be noted whether a sufficiency exists in all trenches occupied, and tins, etc., must be provided for urine and be emptied regularly. The practice common in some units of fouling the trenches must be checked at once. An adequate supply of chlorid of lime and cresol (1½ ounce to 1 gallon water) must be used twice daily by the sanitary details of the companies. Disposal of excreta and other waste will be by burial, except in rearward areas where incinerators are available.

(b) Food Waste: Sandbags will be provided in every bay or convenient length of trench, and at various places in strong points and at dugouts in lines of reserve battalions, in which all empty tins, bread crusts, tea leaves and other waste from kitchens or from the feeding of the men, will be placed at the time. Men found fouling the ground by throwing out waste of this kind will be brought up for punishment. The same rule will be enforced as to old cloths, sandbags, and any other litter.

(c) Water Discipline: All water bottles will be cleaned once weekly by washing with strongly over-chlorinated water which should stand in the bottle for an hour. Every effort will be made to furnish water only from the sources approved, particularly for the front and support line trenches.

(d) Vermin and Flies: The sanitary section of the unit at the time occupying dugouts, tunnels in bluff or spoilbank, or in strong points or elsewhere, will each day remove sandbags, clothing and other litter from the dugouts or other sleeping places, and spray floors, canvas beds, etc., with cresol (7 ounces to 1 gallon water). Sprays have been issued, and can be renewed if necessary from divisional sanitary officer. Nothing short of daily vigilance will control the plague of both flies and lice at this season of the year.

(e) Stagnant Water in Trenches: Apart from other considerations, this tempts the men to fouling of the trench. Where drainage is not convenient, sump holes at the necessary intervals under the trench mats can be baled out as needed and the trenches kept dry at this season.

The medical officers and sanitary sections of units will see to it that their responsibility both in an advisory capacity, and for the work itself, so far as they are responsible for it, is carefully discharged. Persistence and tact in co-operating with unit, company and platoon commanders will at once effect marked improvement.

These instructions, in so far as they can apply, will be enforced in all rearward areas, and by all units in the division, particularly in gun-lines and in wagon and transport lines, and in camps and hutted areas generally.

J. T. FOTHERINGHAM, Colonel,
A. D. M. S., 2nd Canadian Division.

Sanitary requirements, of course, with regard to the methods employed when the division breaks up and starts to travel 60 or 80

miles across country, are another thing. I would like to read you about a dozen lines of instructions issued on that occasion:

August 19, 1916.

O.'s C. Field Ambulances. M. O.'s i/c Units.

Memorandum Regarding Move.

The following suggestions are made for your attention and will be respectfully brought to the attention of your commanding officer.

Sanitation.—No rear parties will be left, and all lines will be carefully cleaned and rubbish buried or placed in incinerators which will be left burning, if not taken over by the advanced party of unit to follow. Particular attention will be paid to ablution places and latrines and to kitchens and horse lines.

On this march, sanitary sections of units will be responsible for the digging of straddle trenches for use during the long halts. Fouling of ground is not to occur, and trenches will be filled in as columns move off, and debris of food, papers, etc., be buried or burned.

Water.—Water bottles will be filled before "lights out" to prevent the necessity of starting with empty bottles in the morning and to permit of re-filling the carts in preparation for the move next morning. Great care is to be observed in controlling waste of water, surplus left in carts being transferred to dixies or traveling kitchens before going to refill carts.

Stragglers.—Horsed ambulances will be placed in charge of a medical officer and follow in rear of brigade transport. Men falling out on the march, if not provided with a note from an officer of their company or platoon will not be picked up unless plainly in need. They should fall out only at road junctions or intersections if possible. Should the horse ambulances become loaded, they will be emptied at a road junction where motor ambulances will later pick up the men. The motor ambulances not being able to move at the slow pace of a column without damage will start from the last bivouac three hours or more after the rear of the column. They will be in charge of a medical officer detailed by O. C. field ambulance who is responsible only to higher medical authority for the use he makes of the technical side of his command. He is under the orders of the G. O. C. brigade for all other purposes.

I should like to say a word with reference to the ambulance cars and wagons with which the field ambulances of the British army are provided. The old establishment was ten 6-horse wagons. Among the many blessings brought to the army by the introduction of petrol as a motive power is the fact that now these ten ambulances are seven motor ambulances and three of the good old 6-horse ambulance wagons. Some one with much wisdom left us with the old-fashioned horse ambulances. These are absolutely invaluable. They go where motor ambulances cannot go; they go across fields and where there are no roads, and, if the weather be reasonably dry, such temporary roads are most useful until by rain and traffic they become impassable. On the other hand, the motor ambulance carrying four lying patients is equally indispensible.

The Motor Ambulance Convoy (M. A. C. for short) is another development of this war. It is an A. S. C. unit not medical, with four medical officers attached, with an establishment of 50 motor ambulances. Its administration rests not with the division but with the corps, and it operates under the D. D. M. S. of the corps between main dressing stations of field ambulances and casualty clearing stations. It is thus the most forward unit for medical purposes of those on the lines of communication. With the help of this unit, in the intervals of heavy fighting, rounds are made as by the baker or milkman at fixed hours, day and night, to every main dressing station, and, in many cases, the advanced dressing stations, from which clearing is thus made to the casualty clearing station with the utmost regularity and speed. During heavy fighting, this unit constitutes a valuable reserve from which extra motor ambulances can be detailed to the overworked and struggling field ambulances who are under fire, and can be divided and detailed to different portions of the fighting front as the tide of battle moves from one portion of the line to the other and the wounded become suddenly numerous in one or other portion of the line. While they constitute a very important link in the chain, the other links are equally efficient. I cannot do better than tell you that, in June of this year, when the Messines ridge was finally taken by the British, the men went over the top at 3:30 a. m., and that men in London, going back from their luncheons to their offices, saw the first convoys of wounded coming in at the Charing Cross station at 3:15 p. m., surely a triumph of organization and evacuation — men back in London in less than 12 hours from the time when they were wounded at the front in Flanders. One hundred dollars a minute could not produce that sort of accommodation in civil life, but the military organization there is so complete and runs so smoothly that a transportation triumph of that sort is possible.

To revert for a moment to the horse ambulances. They are most useful on the line of march, being able to proceed without damage at the pace of a moving column of infantry. Attempt to do this with motor ambulances results in great damage to the vehicles as any one can understand, but, in placing the horse ambulances for the use of moving columns, let me warn the medical officer that if he takes the orders of his brigadier and forgets that ambulance wagons are just as much technical equipment as dressing forceps or scalpels, and therefore not under the brigadier's orders, he will probably find the

stragglers much more numerous than they need be. The brigadier will probably wish an ambulance wagon in rear of each battalion, and the sight of the lumbering vehicles tempts the soldier who thinks he is tired to fall out before his time. We usually allowed a man to fall out, if necessary, at road intersections, and an ambulance wagon which became loaded was permitted to disgorge its load at a road intersection, to be picked up later by the motor ambulances following two or three hours in rear.

If you are not weary, I should like now to take you into the Somme with me and give you one other glimpse of the kind of things for which medical officers are responsible. The first is a copy of the order issued for the training of ambulances in a period of two weeks after leaving the Ypres salient, where we had been for 11 months, and starting on our trip to the Somme in the middle of August, 1916. I shall read you the memorandum on training which I issued for those two weeks.

August 24, 1916.

O.'s C. Field Ambulances, 2nd Canadian Division.

Memorandum on Training.—During the period in the training area, ending on September 4, the following syllabus will be carried out in principle, details being left to officers commanding. It is intended that as technical work will be very light, all ranks shall be fully employed at the military training from which they have been debarred by the pressure of technical duties since arrival in France.

Particular attention will be paid to the military side of the training of all officers, who will take part in all drills and parades.

The following points will be taken up:

1. Squad and company drill.
2. Kit inspections.
3. Guards and sentries.
4. Ceremonial drills and parades.
5. Paying of compliments.
6. Wagon drill.
7. Route marches.
8. Sudden moves by night by sections with transport and loads. Training in making of rendezvous by night, sections moving by different roads.
9. Reconnaissance rides by officers for selection of bivouacs and of field ambulance locations. A report will be submitted by each officer to the O. C. for the A. D. M. S. At least two such rides will be held.

(Signed) J. T. FOTHERINGHAM, Colonel,
A. D. M. S., 2nd Canadian Division.

The fighting on the Somme, as you know, was very concentrated, and much good fighting was done. The Canadian corps went in in four divisions, that is, roughly, 80,000 strong. Of that 80,000, just under 50,000 were infantry. Of course, they were not all put in at once, but half at a time and the other half held in reserve for emergency and for relief. The front was about 1,500 yards, and, being so narrow, our area had to be about 30 miles deep. It was divided into three portions, known as R., S., and T. — R., the rear area, for rest; S., the middle area, for support; T., the fighting area. The support area, or the area in which the field ambulances were kept for rest or hospital purposes, was about 30 miles from the fighting front. In an area of country so congested with troops, roads are at a premium, and only one main road was available for our use, each corps being confined by military police to its own proper roads. Of the 12 field ambulances available from the 4 divisions, 2 were kept in the "rest" area for the care of minor cases of sickness, while others were detailed for the rest stations in the "support" area, and each division, in turn, at the front had its own 3 field ambulances with, usually, the bearers and ambulances of another one on loan from a division not at the time in the fighting line.

We went into the trenches Monday, September 11, and came out on Monday, September 18, at 10 a. m. The casualties in the division for this time were something like 3,000. Practically all of them occurred in the last 76 hours, because the attack began at 6:20 a. m. on Friday, Sept. 15. I need not worry you with details, but I would like to point out before leaving the subject two or three considerations that are of universal application. First is the discovery — and it has never been emphasized in the textbooks, but it is the result of sound experience — that walking and lying cases should never be handled together, nor brought to the same dressing stations. This effects a great saving of time. The rule, as you may know from former wars and still holding good in this war, is that of five men hit, one is killed, one is carried out and the other three can walk out.

Separate arrangements must be made for these two classes — the main dressing station for walking cases, of course, handles the greater number on their way through to casualty clearing station. As an example, I may state that, as I said a moment ago, the men went over the top at 6:20 a. m. on September 11, and at the main dressing station for walking cases which I had established for this fight some 5 miles

in rear of the line and about a mile in rear of the town of Albert, three medical officers, with the necessary assistants of course, from the tent division of one field ambulance, dressed, treated and passed through to the casualty clearing station in the 24 hours between midnight Thursday-Friday and midnight Friday-Saturday no less than 1,637 men, a result which is possible only by sound organization, good discipline and good will. At the main dressing station for lying cases, in the town of Albert, for the same fighting, I had arranged 10 operating tables, each with its proper team of one medical officer and assistants, on a relay basis, for every 8 hours, so that during the 76 hours before relief of the second division, there were handled a total of 994 cases of all sorts of severe wounds. These men had been carried by hand from 2,400-2,800 yards to a point where the horse ambulances could reach them, and from that point to another from which the motor ambulances were available.

I have here a note as to the total casualties handled by the field ambulances of the 2nd Canadian Division during our first tour after the Somme fighting from Friday, September 15 to Monday, September 18, 1916. The total sick and wounded handled in these days was 3,575.

The casualties occurring in the personnel of the field ambulances during that time were: Killed, one officer and 11 other ranks; wounded, one officer and 9 other ranks. The officer killed was Lieut. Col. R. P. Campbell of Montreal, whom I had placed in charge of 450 bearers to control the collection and transport of wounded from the points where they fell to the advance dressing stations at which horse ambulances could reach them. We had not been getting reports as we wished, and early on Saturday morning, wishing to know about conditions at the front trenches, he went up himself instead of sending up a note by some of the bearer parties, to which a reply could be given by some of the medical officers at the regimental aid posts. He knew, of course, the conditions under which these men had been working for the previous 24 or 36 hours, and probably thought that they were too preoccupied to send up frequently the information expected from them. His unselfishness and sense of duty cost him his life, as a piece of high explosive caught him, penetrating the chest under the right collar bone and causing his death in about half an hour, apparently from concealed hemorrhage. He lies buried in the little cemetery outside Albert, and of him it may be said as I think it was said by John

Bunyan of Christian, "And so he passed over. And all the trumpets sounded for him on the other side."

I must finish. There may be some little points about which you would like to know, and if Dr. Belfield, who is chairman, is willing, I shall be glad to answer any question you may ask, if I can.

COLONEL STEPHENSON: It seems to me we are all very much interested in the matter of physical examination. I would like to ask General Fotheringham whether he has any particular word to say about border-line cases and physical examination, particularly about the teeth. A year ago we would not consider accepting a man for a commission who wore a plate. I would like to ask General Fotheringham what is his view about the teeth and plates.

SURGEON-GENERAL FOTHERINGHAM: This is a very live question. We went through the same experience. We followed the British precedent and the British went through the same experience until it became necessary for them to be less exacting in their selection of men.

Under the present system we classify men under five lists, or categories as the official name is.

Category A.—Men who are fit for general service at the front.

Category B.—Men who are fit for service in Britain or France, but not at the front.

Category C.—As in England, the class of those fit for service at home but not overseas. We have the same in Canada.

Category D.—A group of men who being ill at the time, or through defective teeth, or any organic condition, such as hernia, are not fit for service at the time, but can be made available for ordinary service, by medical treatment.

Category E.—Men not fit for any form of military duty.

With reference to the dental question, there is no doubt that the wearing of plates adds to the efficiency of the men in the front trenches. The trouble is that occasionally they intentionally break them in order to get relief from the strain and hard labor of the front, but if a dental laboratory be established, as we had it in the Canadian corps in France, close up to the front, repairs can be executed within 3 or 4 days and the attempt of the soldier to evade duty thus be frustrated. On the other hand, I would not accept for general service at the front men with poor teeth, even though they retain perfectly good health under home conditions. Changes of food, work, exposure, strain, will all add to the handicap under which the man suffers by reason of defective teeth and such a man reaching the front without a plate is not unlikely to break down. A man who has two good opposing teeth in front of the wisdom tooth above and two below on the same side can get along without a plate.

As to heart conditions, I have not had time or opportunity to follow closely the really very excellent work that has been done on that question, particularly in Britain, but the impression I have is that the authorities under the lead of Sir James Mackenzie and others do not allow a purely functional murmur to be a bar if the applicant's health is otherwise good. Certain definite organic murmurs do not preclude service in the lower categories. Certain other organic murmurs, such as mitral stenosis or aortic regurgitation, do exclude from active military employment. The most important thing is the indication as to reserve power of any heart under suspicion by noting the degree of increased rate or

disturbance due to certain specified exercises, such as running up and down stairs, etc., and more particularly the length of time taken by such a quickened heart to resume a normal rate after such exercises. Men, of course, whose hearts are definitely dilated or out of place, especially to the left, are not accepted for any of the higher categories.

QUESTION: How do you handle vermin?

SURGEON-GENERAL FOTHERINGHAM: Under divisional arrangements baths and laundries are provided and placed under the control of a selected officer from one of the units of the division. The "A and Q" side of the divisional headquarters staff arrange that while in brigade or divisional rest all ranks, so far as possible, shall have at least one weekly hot soap and water bath, at which the soiled clothing is exchanged for an issue of fresh. The ordnance issues underclothing and socks only through the divisional bath authorities. The soiled clothing discarded at the baths goes to the laundry, which is usually close by, for sterilization, usually in a steam traveling disinfector. In most divisional baths the outer clothing of the men is freed from lice and eggs while they are in their bath, either by exposure to heat in an improvised steam room or by passing a hot iron along the seams of the garments turned inside out. The latter can be done by securing the services of the peasant women or by employing in this way men physically unfit for duty in the trenches. The ordinary remedies—ointments, powders, etc., advertised for the purpose may be of some service but are quite ineffective to control the situation without a proper system of baths and change of underclothing with disinfection of the khaki.

QUESTION: There was a report in a paper published at Ann Arbor in which it stated that in a regiment of 1,200 men who returned to Canada, about 80% had contracted syphilis. I would like to know if that report is true.

SURGEON-GENERAL FOTHERINGHAM: It is an abominable lie.

DR. PATRICK: I would like to ask if General Fotheringham can give the proportions of his classes, A, B, C, D, and E. A good many of us who have been engaged in examining men have sometimes been perplexed as to what proportion to give to each group.

SURGEON-GENERAL FOTHERINGHAM: I am afraid that I cannot answer that question very well. I can say two or three things about it but would like first to say something more with reference to the last question. I do not doubt that that sort of statement is going around for the reason that such reports have recurred about once a month ever since the war began. They have their origin in the ignorant curiosity and pruriency of the general non-military population. I am prepared to say that the incidence of V. D. among the military is very much less than it is in civil life. You will find it to be just the same with yourselves as with us. If it were not for the disease in civil circles there would be no V. D. among the military. The difference is that we control ours fairly well but practically no effort is made in civil circles to do the same thing. Less than 10% is found among the returned troops and probably half, or more, of that existed prior to the undertaking of military service. Incidence in proportion to the total numbers enlisted is less than 2%.

Reverting now to Dr. Patrick's question, you can quite understand that the proportions of the categories A, B, C, D, and E, will depend partly on whether you are dealing with voluntary enlistments or compulsory. Since we began examining under the Military Service Act, about a month ago, something like

100,000 men have appeared before the medical boards and about 45,000 of them have been placed in Category "A."

DR. CHENEY: Are the reports true of the large proportion of cases of insanity in the men returning from the front?

SURGEON-GENERAL FOTHERINGHAM: We have sent to the front about 300,000 men. We have had back so far about 300 insane, that is one in a thousand. In a complete analysis of 50 of those cases it was found that in only two was alcohol the cause. There is the usual proportion of dementia praecox cases.

DR. GRULEE: Is deafness frequent?

SURGEON-GENERAL FOTHERINGHAM: No, there is not a very great deal of deafness. I should think Dr. J. Gordon Wilson can answer that better than I can, as he has had some months hospital experience overseas in his specialty.

DR. GRULEE: The statement was made that 10% of the men were rendered deaf by concussion.

SURGEON-GENERAL FOTHERINGHAM: Nothing like that.

TRAUMATIC SHOCK

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November 15, 1917

The history of traumatic shock during the past thirty years has been marked by hypotheses that have caused much confusion. These hypotheses give as the cause of shock (1) the exhaustion of the vasomotor center; (2) the excitation of sensory nerves; (3) a hydrostatic fall in blood pressure; (4) vibration injuries; (5) direct wounds of the vasomotor apparatus, and (6) hemorrhage. Some of these ideas are erroneous; others are imperfectly grasped.

The exhaustion of the vasomotor center cannot be the cause of shock because the center does not become exhausted.[1] In shock, it still reacts to the stimulation of the depressor nerve. The fall in blood pressure is great enough to prove that the vasomotor center is not significantly impaired. If the blood pressure remains below the nutrient level for many hours, even the resistant vasomotor center suffers, like all other tissues, though the vasomotor center shows a surprising vitality. But the result of prolonged shock is not to be confused with its cause.

Excitation of sensory nerves is not the cause of shock, because the sensory nerves, in normal animals, may be strongly stimulated for many hours without producing a noteworthy fall in blood pressure.[2]

The confusion of thought that led to the hypothesis of shock from irritation of the nerves rests partly on the mistaken ideas that wounds are acutely painful and that pain per se is followed by shock. Fresh wounds are rarely very painful and shock is seldom preceded by excessive pain. When pain precedes shock, the pain is not necessarily causative.

It is true that a condition roughly resembling shock has occasionally followed an injury to a nerve during an operation. This condition is probably not shock, but a prolonged inhibition of the heart.

It is naturally surprising that a stimulus to a nerve ordinarily innocent, should in such instances call forth strange results. The explanation is that the patient is in a state for which I propose the

[1] Porter, W. T., and Quinby, W. C.: Am. Jour. Physiol., 1908, 20, p. 500.

[2] Porter, W. T.; Marks, H. K., and Swift, J. B., Jr.: Am. Jour. Physiol., 1907, 20, p. 444.

name sensitization. This conception, which is new, rests on experimental evidence. Examples follow: (1) In 50% of dogs given morphin and curare, ligation of the ramus descendens of the left coronary artery produced fatal fibrillation of the heart, whereas fibrillation very rarely occurred when ether alone was used;[3] (2) in a rat to which morphin and curare were given, gently lifting the sciatic nerve on a thread caused inhibition of the heart lasting over half an hour;[4] (3) in the tortoise heart, a stimulus which ordinarily caused a tonus contraction lasting 30 seconds, caused in this case a contraction lasting 64 minutes.[5]

Since the heart is a modified blood vessel, the sensitization of the heart would lead us to expect sensitization of the arteries. I have at present no experimental evidence of this. Yet there is some clinical evidence of prolonged contraction or relaxation of the blood vessels following stimuli ordinarily uneventful. Such is the tonic arterial contraction in certain migraines, and the long relaxations in urticaria. But the evidence in hand, unquestionable for sensitization of the heart, does not as yet warrant including sensitization of the arteries among the sources of confusion in shock.

A simple hydrostatic fall of blood pressure is not shock. When the intestines are exposed, the largest vascular area in the body dilates and the arterial presure falls. If this low pressure continue long enough to impair the nutrition of the vascular apparatus, shock may occur. An admirable example of the hydrostatic fall of blood pressure is seen when a spinal injection of novocain reaches the splanchnic nerve cells. The arterial pressure falls to the shock level, but the fall is usually too transitory to cause shock.[6]

Vibration injuries may cause shock when the vibration, as in certain railway cases, shakes the vasomotor cells until their function is impaired. The blood presure then falls, and if the vibration has been sufficiently severe, the classical symptoms of shock will soon appear. If the injury affects only the lower half of the spinal cord, the vessels of the lower extremities may be dilated for several days, but this vascular area is too small to lower greatly the general blood pressure, and shock does not take place.

[3] Porter, W. T.: Jour. Exper. Med., 1896, 1, p. 49; Arch. f. d. ges. Physiol., 1893, 55, p. 366.

[4] Porter, W. T.: Harvey Lectures, 1906-1907, pp. 113 and 114.

[5] Porter, W. T.: Am. Jour. Physiol., 1905, 15, p. 9.

[6] Porter, W. T., and Smith, G. G.: Am. Jour. Physiol., 1915, 38, p. 108.

Wounds of the vasomotor paths from shell fragments have been observed in this war. If in the abdomen, the interruption to the tonic constrictor impulses is serious. Hydrostatic shock may follow.

That hemorrhage is not usually a cause of shock is proved by the simplest reflection. In the present war, shock occurs approximately once in every hundred casualties. Sometimes the shock case bleeds freely, sometimes not. But practically always, in the other 99 cases, who do not have shock, there will be men who have lost more blood than the shock case.

The idea that hemorrhage is a frequent cause of shock rests on the unquestioned fact that on the operating table the loss of a small quantity of blood is sometimes followed by shock. The explanation is that the blood pressure was near the critical level and that the loss of a small quantity of blood carried the pressure below the critical level. Ordinarily, the loss of from 500 to 1,000 c.c. of blood may leave the pressure still on the safe side of this level.

The critical level of blood pressure is that point below which the blood pressure will not usually rise again without assistance. With the Vaquez instruments used by me in France, the normal diastolic pressure was 97, and the critical level about 60, i. e., between two-thirds and three-fifths of the normal. Certainly, the normal diastolic pressure varies with the instrument employed. It is possible that the critical level shows a similar variation.

An understanding of the critical level is of the first importance in the study and treatment of shock. If the blood pressure just touches the critical level, a difference of 10 mm. of mercury may be the difference between life and death. A few millimeters above this level, recovery will usually occur spontaneously; a few millimeters below, death will follow unless skilled aid be at hand. It follows from this vital fact (1) that procedures which at ordinary blood pressures are not harmful, or are but slightly harmful, may kill the patient at the critical level; (2) remedies that raise the blood pressure but 10 or 15 mm. will save the patient when this rise carries the blood pressure from just below to just above the critical level.

The critical level varies with the condition of the nerve cells and other tissues. A blood pressure high enough to maintain a sufficient nutrition in normal bulbar nerve cells is too low to maintain life in cells that have already suffered from malnutrition. In that case a blood pressure raised by the surgeon to a point above the usual critical

level will shortly sink again. Hence the importance of frequent readings, of the blood pressure until shock patients are clearly out of all danger. Treatment not based on repeated readings of the blood pressure is not intelligent and may be harmful.

The diastolic blood pressure should be employed in shock. In this condition, the heart beats feebly. The systolic pressure falls more than the diastolic pressure falls. Conversely, when remedies are used, they often raise the systolic pressure more than they raise the diastolic pressure. Conclusions drawn from the systolic pressure may easily err 15 mm. or more. But in shock, the blood pressure is at a critical level; a change of even 15 mm. may be a matter of life or death. The error in using the systolic instead of the diastolic pressure may therefore do much harm.

In the summer of 1916, during my service in the fighting line in France, I learned that in this war, shock occurs chiefly after shell fractures of the femur and after multiple wounds through the subcutaneous fat. In 1,000 casualties, observed by me at the Massif de Moronvillers, these were the only injuries producing shock, except certain abdominal wounds in which the shell fragments undoubtedly disturbed the apparatus of the largest vascular area in the body.

It has long been known that fat embolism takes place after fractures of the thigh and after multiple wounds through the subcutaneous fat.

In February, 1917, I proved that the injection of a small quantity of neutral olive oil in the jugular vein was followed by a falling blood pressure and the other symptoms of traumatic shock. The resulting publication was the first clear statement that shock as seen on the battlefield is frequently caused by fat embolism.[7]

Shortly thereafter I developed a new remedy for the treatment of shock. It has long been known that the pumping action of the diaphragm is an important aid in the movement of blood from the abdomen into the chest. At the height of a strong inspiration the venous pressure in the chest may be more than 40 mm. lower than the venous pressure in the abdomen. I produced strong respiratory movements of the diaphragm by allowing the animal to breathe an atmosphere rich in carbon dioxid. The diastolic arterial pressure was thereby increased 15 and even 30 mm.[8]

[7] Porter, W. T.: Boston Med. and Surg. Jour., 1917, 176, p. 248.
[8] Porter, W. T.: Ibid., p. 699.

In June, 1917, at the Chemin des Dames, I successfully applied this new method to the treatment of wounded soldiers. In cases almost pulseless, cases in which all other means of raising the blood pressure had failed, the carbon dioxid respiration strengthened the pulse and raised the diastolic blood pressure 10 mm.[9] This rise is of great value when the pressure is at the critical level.

The general treatment employed by me at the Chemin des Dames was as follows: A shock room was made next the operating room. The patient was carried to the shock room directly from the ambulance. He was not washed. He was at once placed on an operating table, inclined so that the feet were 30 cm. higher than the head. An electric heater was put between the blankets and the body. The diastolic pressure was taken every 15 minutes. When indicated, injections of warm normal saline solution were made into a vein. If his state was grave, adrenalin was added to the saline solution. Carbon dioxid respiration was used. When his condition justified operation, the clothing was cut away about the wound and the area disinfected. Neighboring regions were covered with sterile cloths. He was then moved, still in the inclined position and still on his hot table, to the operating room. The operation was done under local anesthesia, whenever possible. At its close, the patient was wheeled back to the shock room, still on the same inclined, hot table. I did not leave him until he was out of danger or dead. Repeated readings of the pressure were taken. The remedies were directed to raising the diastolic pressure to a point about 15 mm. above the critical level — more is not necessary. One case was operated on during the carbon dioxid breathing, with apparent advantage.

Under these methods four-fifths of the patients recovered.

A word as to details may be of interest. Normal saline solution should be injected at 39 C., measured by a thermometer in the vertical limb of an L-shaped tube placed next the cannula. If the pressure has not remained too long below the critical level, it will be raised by the normal saline; otherwise not, because the permeability of the vessel walls is increased by prolonged low pressures. Professor Bayliss states that the addition of 5% of gum arabic to the saline solution will prevent leakage and thus raise the pressure under all circumstances. This suggestion was made after I had left France, and I have had no personal experience as to its value.

[9] Porter, W. T.: Ibid., 1917, 177, p. 326.

Adrenalin is of temporary advantage, but even this fleeting rise of blood pressure may save life. In the laboratory, the blood pressure of animals may be raised for considerable periods by allowing the well diluted adrenalin to flow into the vein drop by drop from a buret. I have not tried this on men.

Dr. Meltzer very recently stated that the pressor action of epinephrin is much prolonged when the drug is injected into the vertebral canal.

The carbon dioxid respiration should not be stopped too abruptly.

If acidosis be suspected, I am told by eminent authority that 5 grains of sodium bicarbonate should be injected into a vein and the urine be drawn from the bladder. After an hour, the reaction of the freshly secreted urine should be taken. If it is alkaline, acidosis may be excluded, for the time at least. If acid, the urine should again be drawn, and 10 grains of sodium bicarbonate be injected into a vein. If after an hour, the newly excreted urine is still acid, more sodium bicarbonate can be given by the mouth. I have not studied this treatment personally.

ANNOUNCEMENTS

At the annual meeting of the Institute, Dec. 4, 1917, J. B. Herrick, W. A. Pusey, and C. D. Wescott were elected governors for five years, and W. T. Belfield for four years, to take the place of Frank Johnson, resigned.

In accord with the recommendation of the Institute at its October meeting, the board of governors have elected Surgeon-General J. G. Fotheringham, C. M. G., acting director-general, medical services, Canada, honorary fellow.

At the annual meeting of the board of governors, Julius Stieglitz, professor of chemistry in the University of Chicago, was elected president of the Institute, and Robert H. Babcock, vice president. Frank Billings was elected chairman of the board of governors, Joseph A. Capps treasurer, and J. Gordon Wilson secretary. J. B. Herrick is the treasurer in the absence of the treasurer on service.

The board of governors have remitted the dues of all fellows while in active service in the U. S. Army or Navy.

The following have been elected fellows of the Institute: Frank Wright, Emory Hill, F. E. David, Richard Dewey, Fred. B. Noyes, and J. Wendell Clark.

FUNDAMENTAL REQUIREMENTS OF HUMAN NUTRITION *

H. C. Sherman
Professor of Food Chemistry in Columbia University, New York
February 27, 1918

From the standpoint of chemical composition of the diet the fundamental requirements of human nutrition may be considered under the headings of (1) energy value, (2) protein content, (3) inorganic elements, and (4) food hormones or vitamins.

ENERGY REQUIREMENT

So well do the results of different investigators agree regarding the fundamental principles of the energy metabolism and in their quantitative estimates of the basal metabolism of normal men, that one may not only accept their average results as expressing the basal energy requirement with a satisfactory degree of exactness but also may bring together the measurements made in different laboratories on the energy output under various conditions of work and rest so as to furnish a table of hourly rates of energy expenditure from which the daily requirement may be computed.

Reduced to a common basis of 70 kg. of body weight (154 lbs. without clothing) and averaged in round numbers, the data thus compiled are as shown in Table 1. These are the averages of data published at various times during the past several years, chiefly by Atwater and Benedict, Lusk and DuBois, and Becker and Hämäläinen. In view of the emphasis recently placed on the "basal metabolism" as a starting point for computations of energy requirements, the data in Table 1 require further consideration with reference to their relation to the present definition of basal metabolism. General usage now defines basal metabolism as measured when the individual is lying at complete rest and before taking food in the morning. The expression is assumed to imply that at least 12 hours have elapsed since the eating of the last meal so that at least the active period of digestion, absorption, and distribution of digestion products to the tissues has passed. Thus, Benedict refers to basal metabolism as measured in a post-

* Part of the subject matter of this lecture is taken from that delivered before the Harvey Society, New York, Jan. 12, 1918.

absorptive state, and Lusk discusses the effect of food ingestion on metabolism as something apart from basal metabolism. The averages given in Table 1 are, however, derived chiefly from data of experiments in which the subjects received sufficient food for maintenance, and in some cases for the support of muscular activity as well. The data for energy expenditure during sleep as given in Table 1 are chiefly from measurements taken during periods of 3, 4 or 6 hours beginning at 1 a. m. and are therefore presumably somewhat affected by the specific dynamic action of the food taken at the evening meal and therefore slightly higher than they would be if separated from the last meal by a period of 12-14 hours as in most of the measurements of

TABLE 1

HOURLY EXPENDITURE OF ENERGY BY AVERAGE SIZED MAN (70 KG., 154 LBS. WITHOUT CLOTHING) UNDER DIFFERENT CONDITIONS OF ACTIVITY. (APPROXIMATE AVERAGES ONLY.)

Condition or Occupation	Number of Calories
Sleeping	60–70
Awake, lying still	70–85
Sitting at rest	100
Standing at rest	115
Tailoring	135
Typewriting rapidly	140
Bookbinding	170
Light exercise (bicycle ergometer)	170
Shoemaking	180
Walking slowly (about 2⅝ miles per hour)	200
Carpentry	240
Metal working	240
Industrial painting	240
Active exercise (bicycle ergometer)	290
Walking actively (about 3¾ miles per hour)	300
Stoneworking	400
Severe exercise (bicycle ergometer)	450
Sawing wood	480
Running (about 5¼ miles per hour)	500
Very severe exercise (bicycle ergometer)	600

basal metabolism. In some cases the energy metabolism during sleep is also increased by the after-effect of muscular work performed during the preceding day, as shown by Benedict and Carpenter. Similarly the energy expenditure for subjects awake but lying still will range from the basal rate upward according to the extent to which the energy output is influenced by the after-effect of food or of muscular activity, or by the tendency noted by Benedict[1] toward increased energy metabolism as the waking day advances even when no food and little muscular exercise is taken.

Lusk[2] summarizes the experimental evidence regarding basal metabolism as follows:

[1] Publication No. 203, Carnegie Institution of Washington.

[2] Science of Nutrition, Ed. 3, p. 127.

"The new formula (of DuBois for computing body surface) gives the following results, the subjects being men between the ages of 20 and 50 years:

	Average Calories per Square Meter per Hour
Average of 9 normal controls (DuBois[3])	39.7
Average of 9 normal controls (Means[4])	39.6
Average of 82 normal controls (Benedict[5])	38.9

If the average man be taken as having a weight of 70 kg. (154 lbs. without clothing), a height of 173 cm. (5 ft. 8 in. without shoes) and a body surface of 1.83 sq. meters (DuBois chart), then his average basal metabolism would be 38.9-39.7 calories per hour per sq. meter of surface, or 71-73 calories per man per hour, or 1.01-1.04 calories per kg. per hour in the conditions chosen for measurement of basal metabolism. Under ordinary conditions the effect of food and the other effects above mentioned may raise this rate of energy expenditure to any extent up to perhaps 85 calories as indicated in Table 1 as a maximum for a normal man of 70 kg. when awake, lying still under ordinary conditions.

For the case of a healthy man or woman of normal physique the energy requirement for a day of 24 hours can be calculated from the data given in Table 1, multiplying the hour rate of calory expenditure by the number of hours spent in each different condition or activity, adding the products and reducing or increasing the total number of calories thus found according as the actual body weight is less or more than 70 kg. If the degree or intensity of muscular activity is correctly interpreted, the results thus computed will be found entirely consistent with the now generally accepted estimates of the food requirements of people of different occupations, and with the data which one obtains by the use of the charts recently constructed by Lusk.*

Lusk's general method of calculating the energy requirement of the day is as follows: Starting with the basal rate, he first adds 10% for those hours in which the subject is out of bed. Assuming 8 hours in bed and 16 hours sitting up the basal rate per hour would first be multiplied by 24 and then by 1.067. To this result must then be added the extra calories of metabolism due to occupation. In estimating that the metabolism when out of bed at rest is only 10% above the basal rate,

[3] Arch. Int. Med., 1916, 17, p. 902.
[4] Jour. Med. Research, 1915, 32, p. 121. Jour. Biol. Chem., 1915, 21, p. 263.
[5] Jour. Biol. Chem., 1914, 18, p. 139.
*Lusk's charts have now been published in the Jour. Am. Med. Assn., 1918, 70, p. 821.

Lusk assumes that no food has been taken, and he therefore arrives at a figure for metabolism when sitting at rest which is lower than that given in Table 1 based chiefly on the work of Atwater and Benedict, because the latter, as already explained, is the approximate average of actual observations at various times of the day and, in general, on days in which the subject received enough food for maintenance, or in some cases to support a considerable amount of work. A part of the specific dynamic action of one of the 3 meals, which together furnished 2,000 to 3,500 calories daily, would therefore appear in the data for hours of rest as published by Atwater and Benedict and included in Table 1. Offsetting this difference in mode of expressing the results is the fact that in calculating the day's requirement for people of different sizes, Lusk[6] uses average weights which include ordinary clothing, whereas the data of Atwater and Benedict and the estimates summarized in Table 1 are based on body weight without clothing.

These differences in treatment of the factors of food and clothing in the two modes of calculation offset each other in such a way that any discrepancies which may seem to exist become for practical purposes apparent rather than real, the final results of the two methods being essentially alike. Thus Lusk's chart indicates that a carpenter weighing, with clothing, 163 lbs. will require 3,260 calories per day, while the writer's calculation[7] from the data of Table 1, indicated for a carpenter of the same size (154 lbs. without clothing) a requirement of 3,380 calories per day. This difference of about 3% may be considered negligible so far as practical applications are concerned since it is no greater than the variations in energy value which must be expected between successive specimens of most staple articles of food. Furthermore, Lusk suggests that perhaps 200 calories per day for men and 150 for women should be added to the estimates shown on his charts, as an allowance for incidental muscular movements of the non-working hours of the day. In the case of the carpenter just discussed, such an addition would bring the results of the two calculations of energy requirement into still closer agreement.

It seems safe to say that at the present time there are no important differences of opinion regarding the energy requirement for the maintenance of what is commonly regarded as the normal condition of nutrition in human adults or for the support of the familiar forms of mus-

[6] Science of Nutrition, Ed. 3, p. 821.
[7] Sherman: Chemistry of Food and Nutrition, Ed. 2, p. 186.

cular activity in so far as muscular work can be described in quantitative terms.

In view of recent developments the possibility of lowering the basal energy requirement through restriction of the food intake must also be considered. Lusk has cited individual instances of lowered metabolism in undernutrition of human beings and in conjunction with Anderson[8] has investigated the question experimentally with the dog; while Benedict* has simultaneously conducted a large scale experiment on 25 men in which it was found that reductions in amount of food eaten sufficient to reduce body weight about 10% resulted in a more than proportional lowering of energy metabolism. Benedict attributes this lowering of metabolism largely to the fact that the reduction of diet resulted in the elimination of a large amount of "surplus nitrogen" from the body, the loss of body nitrogen in his subjects averaging about 150 gm. The presence in the body of this large amount of "surplus nitrogen" under ordinary conditions of liberal feeding is held to constitute a stimulus to cellular activity which may be removed by dietary restriction without apparent injury to the organism and with distinct saving in food consumption. Benedict and Smith find that the men when at reduced body weight performed the muscular work of walking somewhat more efficiently than before, whereas Lusk interprets the work of Anderson and Lusk as showing (for the dog) that when a given amount of work is to be done it is always accomplished at the expense of the same amount of extra calories, no matter what the nutritive condition of the animal may be.[9] That the two investigations should yield results differing on this one point only need not materialy modify our position that there is now substantial agreement among authorities on nutrition regarding both the qualitative and quantitative aspects of the fundamental problems of the energy requirement.

Both Lusk and Benedict emphasize the high energy requirement of children and would rigidly confine to the adult members of the community any possible attempts to "economize on calories."

The available data on the energy requirements of growing children† are less concordant than the data for adults, so that average figures analogous to those for adults in Table 1 are more difficult to give for

[8] Jour. Biol. Chem., 1917, 32, p. 421.

[9] Jour. Am. Med. Assn., 1918, 70, p. 823.

* Only preliminary announcement of Benedict's results has yet been made. The full account is to be published by the Carnegie Institution of Washington.

† Data available up to 1916 are summarized in Gillett's Food Allowances for Healthy Children (New York Association for Improving the Condition of the Poor, 1917).

children, and would be less accurate to use. DuBois has constructed a curve of basal metabolism per sq. meter of body surface at different ages, but the condition predicated for the measurement of basal metabolism—complete quiescence on an empty stomach—is so remote from the usual status of a healthy growing child, that it is necessary to make large assumptions in arguing from the rate of the basal metabolism to the total requirement for a day of normal activity. Estimates of the energy requirements of healthy children must therefore allow for considerable individual variations.

It is necessary in making food allowances for individual children to exercise much judgment as to the activity of the child and also as to whether he is maintaining not only a normal rate of growth in

TABLE 2

FOOD ALLOWANCES FOR HEALTHY CHILDREN (GILLETT)

Age, Years	Calories per Day	
	Boys	Girls
Under 2	900–1,200	900–1,200
2– 3	1,000–1,300	980–1,280
3– 4	1,100–1,400	1,060–1,360
4– 5	1,200–1,500	1,140–1,440
5– 6	1,300–1,600	1,220–1,520
6– 7	1,400–1,700	1,300–1,600
7– 8	1,500–1,800	1,380–1,680
8– 9	1,600–1,900	1,460–1,760
9–10	1,700–2,000	1,550–1,850
10–11	1,900–2,200	1,650–1,950
11–12	2,100–2,400	1,750–2,050
12–13	2,300–2,700	1,850–2,150
13–14	2,500–2,900	1,950–2,250
14–15	2,600–3,100	2,050–2,350
15–16	2,700–3,300	2,150–2,450
16–17	2,700–3,400	2,250–2,550

weight, but also a desirable ratio of height and weight; in other words, a desirable degree of fatness. Children who are under weight for height and age may need more food calories than either their height or their age would normally indicate. Either for this reason or (as in the case of the school boys found by Gephart to consume 5,000 calories per day) to provide for exceptional activity in certain individuals, it may sometimes be best to provide more calories than shown in Table 2; but this is believed to be the best guide at present available for use in computing energy allowances for healthy children living under ordinary conditions.

In computing the results of dietary studies to the basis of nutrients and calories "per man per day" it has been the custom in this country for several years to calculate the relative food consumption of chil-

dren to the "man" basis by means of the second set of factors proposed for this purpose by the late Professor Atwater according to which:

A boy of 15-16 years averages 0.9; a boy of 13-14, or girl of 15-16, 0.8; a boy of 12, or girl of 13-14, 0.7; a boy of 10-11, or girl of 10-12, 0.6; children of 6-9, 0.5; children of 2-5 years, 0.4; children under 2 years, 0.3 of the amount of food consumed by an average man at moderately hard muscular work, which was estimated at 3,500 calories per day.

It should be emphasized that the factors thus used in computing food of children are decimal fractions of 3,500 calories and do not by any means necessarily express the relation of the child's food requirement to that of its father. Men do not require so much as 3,500 calories unless engaged at fairly heavy muscular work. The estimated requirement of the carpenter, which served as illustration in the foregoing, was not so high as this, and men at sedentary or professional occupations are usually considered to require about 2,500 calories per day.

As an approximate indication of average need or as a basis for the discussion of the adequacy of other factors of the diet, it is more or less customary to assume 3,000 calories per man per day as a norm. But if the decimal fractions previously cited be applied to 3,000 calories, instead of 3,500 calories as intended, it is obvious that the resulting data will be about 15% below the average needs of normal children. While the use of the decimals as factors is a convenience in calculating the results of dietary studies, it seems safer in computing food requirements of family groups to allow for the needs of each child on its own merits directly in terms of calories per day.

PROTEIN REQUIREMENT

The protein requirement has not been so accurately and conclusively measured as has the energy requirement. Chittenden's well known investigation of over a decade ago[10] remains the largest single contribution to this subject and the criticisms evoked at the time by his advocacy of a standard for protein consumption only a little higher than the rate of catabolism shown by his observations — corresponding to 44-53 gm. of protein per man of 70 kg. per day—are perhaps as suggestive as any which have been offered. Notable among these criticisms were Maltzer's argument[11] that the usual high rate of pro-

[10] Physiological Economy in Nutrition and The Nutrition of Man.
[11] Harvey Lectures for 1906-1907, p. 139.

tein consumption constitutes an important factor of safety which it would be a mistake to forego by reducing the protein content of the ration to a figure near the minimum requirement, and Benedict's criticism[12] of the low protein diets as likely to be accompanied by a less complete digestive utilization of the nonprotein food. In connection with the latter point it is interesting to note that Mills[13] found a better ultilization of subcutaneously injected fat when the experimental animals (cats) were fed a high protein diet than when they were fed on low protein or fasted. Mills suggested that this might be because the high protein furnished more lipase in the body, and Falk and Siguira[14] found that their (castor bean) lipase preparations were composed essentially of protein material, as had already been shown in the case of purified preparations of both plant and animal amylases.[15, 16, 17]

TABLE 3

FORMS OF NITROGEN IN PROTEIN MATERIALS AND ENZYME PREPARATIONS. (EXPRESSED IN PERCENTAGE OF THE TOTAL NITROGEN IN THE MATERIAL.)

Form of Nitrogen	Casein[1]	Edestin[1]	Hemo-Glogin[1]	Hair[1]	Pancreatic Amylase[3]	Malt Amylase[2]	Castor Bean Lipase[3]
Arginin N	7.4	27.0	7.7	15.3	14.6	14.2	24.7
Histidin N	6.2	5.8	12.7	3.5	6.0	5.4	6.2
Lysin N	10.3	3.9	10.9	5.4	7.4	5.5	4.3
Cystin N	0.2	1.5	?	6.6	2.5	4.9	3.1
Amino N of filtrate	55.8	47.5	57.0	47.5	50.4	52.4	49.4
Nonamino N of filtrate	7.1	1.7	2.9	3.1	4.6	4.5	....
Ammonia N	10.3	10.0	5.2	10.0	8.1	7.9	12.1
Melanin N	1.3	2.0	3.6	7.4	5.3	5.6	3.3

1. Van Slyke (1910).
2. Sherman and Gettler (1913).
3. Falk and Siguira (1915).

The forms of nitrogen distinguishable by the Van Slyke method are shown in Table 3 for a number of typical proteins or protein tissues and for purified amylase and lipase preparations.

Since the criteria of purity ordinarily used in chemical research are not applicable to unstable coloidal substances like the digestive enzymes, it is easy to say that such preparations may be far from pure. It has even been suggested that the protein matter of which these enzyme preparations chiefly consist may be only an impurity or a

[12] Am. Jour. Physiol., 1906, 16, p. 409.
[13] Arch. Int. Med., 1911, 7, p. 694.
[14] Jour. Am. Chem. Soc., 1915, 37, p. 217.
[15] Osborne: Jour. Am. Chem. Soc., 1895, 18, p. 587.
[16] Sherman and Schlesinger: Jour. Am. Chem. Soc., 1912, 34, p. 1104. 1915, 37, p. 1305.
[17] Sherman and Gettler: Ibid., 1913, 35, p. 179.

"carrier" while the "real enzyme" is something of wholly unknown chemical nature. There is, however, no positive evidence in support of this latter suggestion. On the other hand, there is much evidence which, while not conclusive, is direct and positive in character, tending to show that the common hydrolytic enzymes, such as those concerned in the utilization of foodstuffs, either are proteins or contain protein matter as an essential constituent.

Probably therefore the food protein must furnish material for body enzymes as well as for body tissue. Both this consideration and the more familiar one that individual amino-acids furnished by the food proteins may serve as precursors of body hormones,[18, 19] naturally tend toward caution in the acceptance of a low protein standard, especially since the proteins have been shown to vary widely in their amino-acid make-up and in their nutritive value when fed singly, especially in experiments on growing animals.[19, 20]

These differences in nutritive value among proteins especially as correlated with chemical structure by Osborne and Mendel, are of the greatest importance, but we should be careful not to mistake them as justifying a needless degree of timidity in accepting and applying the results of experiments on the amount of protein required for normal human nutrition. Rather they furnish us the information necessary to enable us to plan economical use of protein wisely and with confidence. When food is to be used economically the best guide to the amount of protein needed is the result of experiments, made with men, to find the smallest amount on which one can subsist without continuously drawing on his body stores, as shown by the nitrogen output.

The nitrogen output on a diet markedly deficient in protein and involving a large loss of body nitrogen may be less than the nitrogen requirement since a large nitrogen loss from the body might not be convertible to equilibrium by the addition of an equal amount of food nitrogen to the intake; but when there is nitrogen equilibrium on a low protein diet it seems safe to conclude that such diet is meeting all the demands of normal maintenance so far as protein is concerned. Also when the nitrogen output is only very slightly greater than the intake it seems permissible to regard the output as approximating the actual requirement.

[18] Willcock and Hopkins: Jour. Physiol., 1906, 35, p. 88.

[19] Osborne and Mendel: Jour. Biol. Chem., passim.

[20] Osborne and Mendel: Carnegie Institution of Washington, 1911, and subsequent papers in Jour. Biol. Chem.

We have therefore thought it worth while to bring together the data of all experiments of which we found record in which the dietary conditions and the nitrogen balance were such as to indicate that the output of nitrogen might be reasonably construed as approximating the actual nutritive requirement. In order to minimize the personal equation in interpretation we have uniformly excluded all experiments showing a loss of nitrogen greater than 1 gm. per day. There remained 86 experiments on adults showing no abnormality of digestion or health, in which the diet was sufficiently well adjusted to the probable requirement and the nitrogen balance showed sufficient approach to equilibrium to make it appear that the total output of nitrogen might be taken as an indication of the protein requirement. These experiments are taken from 20 independent investigations in which 41 different individuals (37 men and 4 women) served as subjects. For purposes of comparison the daily output of total nitrogen in each experiment was calculated to protein and this to a basis of 70 kg. of body weight. Reckoned in this way, the apparent protein requirement as indicated by the data of individual experiments ranged between the extremes of 20.0 and 79.2 gm., averaging 49.2 gm. of protein per man of 70 kg. per day. Thus the average falls well within the range of Chittenden's estimate of the amount of protein required for normal nutrition when the energy value of diet is adequate.

Examination of the data recorded in the original papers indicates that the wide differences in amounts of protein catabolized in the different experiments cannot in these cases be attributed primarily to the kind of protein consumed nor to the use of diets of fuel values widely different from the energy requirements. Apparently the most influential factor was the extent to which the subject had become accustomed to a low protein diet.

In view of the fact that individual proteins when fed singly, especially to growing animals, have shown striking differences in nutritive efficiency,[21] it may seem strange that in the experiments hitherto made to determine the protein requirement of man, the kind of protein fed has not had more influence on the amount required. There is, however, no real discrepancy between the two sets of findings. Experiments like those of Osborne and Mendel, for example, were for the purpose of comparing individual proteins isolated even from the other proteins which always accompany them in natural or commercial food materials, and were conducted largely on rapidly

[21] Mendel: Harvey Lectures for 1914-1915, p. 101.

growing young animals in which there is an active synthesis and retention of protein so that a deficiency in the supply of any amino-acid which is required in the construction of body protein is apt to be quickly and plainly reflected in a diminution or cessation of growth. On the other hand, in experiments the purpose of which is not to compare proteins, but to measure the normal protein requirement, the diet is naturally made up, not of isolated proteins or even of single or unusual foods, but (ordinarily at least) of such combinations of staple foods as are believed to represent a normal diet, so that even a relatively simple ration arranged for the purpose of such an experiment would probably contain a number of different proteins among which any peculiarities of amino-acid make-up would be apt to offset each other at least to a considerable extent. Moreover, the particular experiments on human nutrition now under discussion have been made entirely on adults whose protein requirement was limited to that of maintenance. In such cases there is no longer a demand for amino-acids to be built into new tissue, but only to maintain the equilibrium which already exists between amino-acids and proteins in the full grown tissues. Any of the amino-acids whose radicles are contained in tissue proteins may be expected to contribute something to the maintenance of such an equilibrium, whereas there can be no growth unless all the necessary amino-acids are present. In the protein metabolism of growing children or nursing mothers the influence of food selection would probably be much more pronounced, and even in the case of adult men protein requirement will probably be found to be considerably influenced by food selection when experiments suitably planned to test the question are carried out. The inadequacy of gelatin as a sole protein food and its inferiority to meat or milk protein when substituted beyond a certain proportion is well known. A series of experiments, designed to demonstrate differences in nutritive efficiency for man of the protein supplied by different staple articles of food, was carried out by Karl Thomas[22] in Rubner's laboratory and the striking results reported have been widely quoted, often on Rubner's authority. These results, however, have as yet failed of confirmation, and, on some important points, have been so directly refuted by later workers using longer experimental periods, as to make it appear that Thomas' plan of experimenting and mode of interpretation were not entirely suited to the solution of the question at issue. Thomas thought he had demonstrated that meat protein was

[22] Arch. f. Anat. u. Physiol., 1909, p. 219.

greatly superior to bread or potato protein for the maintenance of body tissue; but Hindhede[23] finds no such striking difference, being able to maintain normal nutrition with either bread or potato nitrogen in relatively small amounts.

Rose and Cooper[24] have also demonstrated the high value of potato nitrogen in the maintenance of nitrogen equilibrium, and experiments in the writer's laboratory[25] have tended to confirm Hindhede's finding that nitrogen equilibrium may be maintained on a relatively low intake of protein in the form of bread.

Of at least equal practical importance are those experiments[26] which show the maintenance of nitrogen equilibrium over long periods on low protein diet in which bread was the chief source of protein but was supplemented by small amounts of milk.

McCollum in 1911[27] called attention to the rather surprising nutritive efficiency of zein in cases in which only maintenance was involved, and offered the suggestion that "repair" processes may not involve the disruption and reconstruction of entire protein molecules. The same idea may be expressed from a slightly different point of view by saying that, having in the cell under conditions of maintenance, an equilibrium between protein and a whole group of amino-acids, the catabolism of protein will be diminished by increasing the concentration of any (even though not all) of the amino-acids into which the protein molecule tends to be resolved.

Thus, food proteins which do not furnish all of the amino-acids needed for the construction of body tissue and which therefore could not properly be made the chief reliance in the feeding of growing children, or of women during pregnancy or lactation, may still be depended on to a very large extent for the ordinary maintenance of adults.

Nor does it seem necessary to assume that because of the differences in nutritive value among proteins, a very large margin for safety must be allowed above the average amount found in the 86 experiments previously cited. This would be true only if the diets in these experiments had been selected from among materials whose proteins are of more than average value, which in general is not the case. In fact, in the low protein diets used in these experiments there

[23] Arch. f. Physiol., 1913, 30, p. 97; 1914, 31, p. 259.
[24] Jour. Biol. Chem., 1917, 30, p. 201.
[25] Sherman, Winters and Osterberg: Unpublished data.
[26] Sherman, Wheeler and Winters: Unpublished data.
[27] Am. Jour. Physiol., 1911, 29, p. 215.

was often if not usually a more than average proportion of bread or other grain protein, so that, if anything, the experiments tend to overstate the amount of protein which an ordinary mixed diet must furnish in order to cover the requirements of normal protein metabolism in the adult. Under these conditions it seems abundantly liberal to allow when planning for an economic use of food, a protein "standard" 50% higher than the average estimate of the actual requirement (which as already shown is probably an overestimate). Such a 50% margin for safety would lead to a tentative standard allowance of about 75 gm. of protein per man per day. The requirements of children for protein as well as other tissue building material will be considered as proportional to their energy requirements and therefore much higher per unit of weight than in the case of adults.

INORGANIC ELEMENTS AND THE FOOD HORMONES OR VITAMINS

Of the 15 or 16 chemical elements which seem to be essential constituents of the body, it is believed that our ordinary food supply, with the table salt commonly added, will carry an abundance to meet nutritive requirements unless in the case of phosphorus, calcium or iron. For several years there have been indications that these 3 elements should not be left wholly to chance but should be reckoned with in considering the adequacy of dietaries. Until recently we had relatively few data as to the amounts of these elements required in nutrition, and this is still true of iron. Moreover, in the case of phosphorus and calcium the data were open to the further criticism of having been determined almost exclusively on male subjects. Experiments on women were therefore plainly needed, and since the effects of the monthly cycle on phosphorus and calcium metabolism had not been studied, it was especially desirable that the determination of intake and output should continue for an entire month without intermission. Four young women, graduate students and research workers in the writer's laboratory, have served as subjects in such experiments, taking diets uniform from day to day for 28 or 30 days, consecutively, with quantitative determinations of intake and output of nitrogen, phosphorus and calcium balanced in experimental periods of 3 or 4 days each.[28, 29]

The determination of phosphorus and calcium balance in 3 or 4 day periods for 28 or 30 days without intermission gave therefore in

[28] Sherman, Gillett and Pope: Jour. Biol. Chem., 34, p. 373 (1918).
[29] Sherman, Wheeler and Yates: Jour. Biol. Chem., 34, p. 383 (1818).

each case a series of 7-10 experiments of unusual value for the purpose of studying the requirement, since the diets were so arranged as to furnish the desired numbers of calories and amounts of protein with quantities of phosphorus and calcium small enough to test the ability of the body to establish equilibrium on the amounts furnished, and to show to how low a level of phosphorus or of calcium metabolism the body could adjust itself.

The minimum requirements thus found, computed, for convenience of comparison and application, to a basis of 70 kg. body weight, corresponded, respectively, to 0.91, 0.72, 0.83, and 0.89 gm. phosphorus, and 0.49, 0.38, and 0.44 gm. calcium "per man per day."

Averaging these results with those of several other experiments made in this laboratory on both men and women and with all comparable data found in the literature, indicates a mean requirement per 70 kg. of body weight of 0.88 gm. phosphorus and 0.45 gm. calcium per day.

TABLE 4

NUTRITIVE "REQUIREMENTS" AND ACTUAL INTAKE PER MAN PER DAY

	Protein	Phosphorus	Calcium
Number of experiments	86	87	63
"Requirements" gm.—			
Range	20.0-79.2	0.52-1.19	0.27-0.78
Average	49.2	0.88	0.45
"Standard" (50% above "requirement")	75 gm.	1.32 gm.	0.68 gm.
Average amounts in 246 dietaries	106 gm.	1.60 gm.	0.74 gm.
Proportion of cases below "requirement"	Less than 1%	4%	16%
Proportion below "requirement" if total food were 3,000 calories in each case	None	2%	12%

Considering both the number of experiments contributing to the average and the range of results in each case, it would seem that our present knowledge of the quantities required for normal nutrition is probably about equally accurate as regards protein, phosphorus, and calcium. This being so, we have as much reason to set phosphorus and calcium "standards" as to set a "standard" for protein, and it seems logical to allow as much margin for safety in the one case as the other. Table 4 summarizes the data on which these estimates of "requirements" are based and shows also the relative frequency of American dietaries which fall below the "requirement" in each case.

It must be stated with all possible emphasis that the words "requirement" and "standard" are used here only for lack of better terms and that they have not and cannot have the unconditional significance which is apt to be attached to them. McCollum's recent

work[30] emphasizes the fact, which earlier work on the metabolism of calcium and iron[31, 32] had illustrated, that the amount of any one nutrient required will depend to a considerable extent on the amounts of other nutrients furnished. In taking the average of the minima of various investigations as an estimate of the "requirement" we do not mean that just this amount will be literally required in each case. The very experiments from which this average is derived are sufficient to show that the minimum of requirement varies with the subject and the diet if not with other conditions. Similarly, if we take an amount 50% above the average minimum as a "standard" it is by no means intended to imply that this amount will be always the most desirable. On the contrary, a larger amount might easily be advantageous, especially in the case of calcium as a safeguard against failure of completely normal absorption in the digestive tract.

Thus, the quantitative statements of what are here called "requirement" and tentative "standard" must not be too literally interpreted nor too mechanically applied. They are, however, directly useful as a concrete basis for classifying the results of dietary studies as to whether they contain liberal or scanty amounts of the element in question. An intake less than the so-called requirement does not necessarily mean a continuing deficit leading finally to disaster in every individual case, but does mean that there is always this danger wherever such low intakes are habitual.

Of the 246 dietary studies referred to in Table 4, 144 were originally recorded by the U. S. Department of Agriculture and have recently been subjected to more detailed analysis and computation, especially as regards the mineral elements, in connection with the investigations on mineral metabolism at Columbia University; 102 were collected and studied in detail by Miss Gillett, working under the joint auspices of the University and the New York Association for Improving the Condition of the Poor. Most but not all of the latter were from New York City. Of the 144 government studies, 54 were made in New York City, 46 in other large cities, 44 in small cities or towns and rural regions. In each of these 4 groups calcium is the element most often deficient and of which the average intake shows the least margin of safety above the bare requirement. It is particularly interesting to note the agreement of this result with that of

[30] Jour. Biol. Chem., passim.
[31] Von Wendt: Skand. Arch. Physiol., 1905, 17, p. 211.
[32] Sherman: Bull. 185, office of Exper. Stations, U. S. Dept. Agricul., p. 37.

McCollum[33] who has found in his studiees of laboratory animals that it is largely because of insufficient calcium intake that such animals do not show normal nutrition on rations derived too largely from seeds. American dietaries, both urban and rural, tend to consist too largely of the product of seeds (breadstuffs, etc.), meats, sugar and fats all of which are poor in calcium — and too little of milk and vegetables which should be used in larger proportion both for their mineral constituents and for the vitamins which they furnish. By separate study of the data of the 44 dietaries studied in small towns and rural regions it was found that here also the adequacy of calcium intake depended chiefly on the amount of milk consumed, adequate calcium being found, on the average, only in those dietaries which contain at least one-third of a quart of milk per man per day.

These results indicate very strongly that the average American dietary contains a much more liberal margin of protein than of calcium, and that while the danger of a protein deficiency is rather remote the danger of an occasional deficiency of calcium is very real.

So far as the actual requirements of the calcium metabolism are concerned, these (as well as the phosphorus requirements) could be met by the addition of simple mineral salts or perhaps of bone flour or bone ash to the food, but since the foods rich in calcium, notably milk, eggs, vegetables and some fruits, are valuable for other properties as well, it seems wiser to encourage the more liberal use of these foods.

The "vitamin" requirement cannot be stated in terms of actual weights of Fat-Soluble A and of Water-Soluble B, but the percentage of certain foods rich in the one or the other of these essentials which suffice to make an otherwise satisfactory diet adequate for normal growth and for reproduction in laboratory animals have been determined experimentally for several food materials by Osborne and Mendel and by McCollum and his associates, so that we now know in a general way the relative richness of several of the chief types of food in each of these dietary essentials and can take account of this factor of food value in considering the prominence which should be given to each type of food in planning an adequate and economical diet.

It is very interesting and important to find how generally the types of food rich in calcium — milk, eggs, vegetables — are rich in vitamins as well, so that in safeguarding against deficiency of the element

[33] Jour. Biol. Chem., passim.

most likely to be deficient, we at the same time secure an ample intake of the food hormones or vitamins.

The use of liberal amounts of fruit and vegetables will also tend to promote intestinal hygiene and to safeguard the antiscorbutic property of the diet.

An excellent series of suggestive meal plans, sufficiently flexible and yet indicating the proper prominence of the different types of food, has recently been published by Professor Rose.[34]

Present knowledge of nutrition and food values shows that it is perfectly feasible to modify the average American dietary in the manner desired by the Food Administration to meet the present emergency conditions and make it a better diet at the same time.

Substitution of corn meal or oatmeal for part of the wheat flour in breadmaking, or of graham or entire wheat for patent flour, or diminished use of bread with correspondingly increased use of potatoes will in any case maintain the nutritive value of the diet and in many cases improve it by increasing the intake of desirable mineral elements and of the vitamins.

Substitution of more perishable foods such as vegetables, fruits and milk, for a part of the meat, sugar and fat hitherto used will be of positive and decided advantage from the standpoint of well-balanced nutrition. Notwithstanding the rise in price made necessary by increased cost of production, there should be no attempt to get along with a lowered milk consumption, but rather an earnest and persistent effort to increase the use of milk in the family dietary.

There is nothing more important in the whole problem of food supply than that the purchase of market milk be fully maintained in order to prevent any depletion of the dairy herds. A liberal use of milk in the diet is the best safeguard against any deficiency which might arise through restricted choice of foods and the safest way to ensure that the consumption of enough food to maintain a normal weight for the height and age, shall meet all other requirements of nutrition as well.

[34] Feeding the Family, New York, 1917.

ANGINA PECTORIS

E. Fletcher Ingals
CHICAGO

March 28, 1918

I do not know of any greater service I can render the fellows of this institute and the public than by considering, from a very intimate acquaintance, the time-worn affection that forms the subject of this article. I cannot hope to add much that is new, but I confidently hope to call attention to vital points that may have been overlooked by some practitioners, though of the highest importance to sufferers from this malady.

Just at the beginning of the world war, Sir Clifford Allbutt published an exhaustive work on diseases of the arteries and angina pectoris, in which he presents many arguments against some of the long-accepted views on these subjects. But the very comprehensiveness of the 2 large volumes places the matter far beyond the time limit of the average practitioner, and almost beyond that of the specialist devoted to diseases of the circulatory organs. A careful study of Allbutt's work and an analysis of 60 histories of angina pectoris, out of the 1,396 cases of heart disease that I find among my records of private patients (exclusive of all dispensary and hospital cases) has considerably modified the views I formerly held on this subject. Many of the patients were seen in consultations with other physicians or came to me from a distance, so that I saw them only once or twice. In most of them I did not learn of the final result, and in very few, because of their being private patients, have I been able to see the pathologic changes. Allbutt has been able to make extensive studies of pathologic changes in this disease; therefore I cannot speak with assurance on points when my former impressions do not coincide with his; but from the clinical standpoint alone I feel confidence in my own observations, and the views I shall present in this paper seem to me sustained by the facts.

SUBJECT AND DEFINITION

Angina pectoris is a paroxysmal painful disease of the circulatory organs in which the pain is usually located near the base of the heart, over the large arteries and in the shoulders, neck and arms, most fre-

The material for this paper was gathered by Dr. Ingals during the past summer; but on his becoming exhausted, he secured the assistance of William R. Meeker, who arranged the material in readable form.

quently confined to the left side, but often in the right side. It is often attended by dyspnea and commonly by mental depression or a sense of impending death, which must not be confounded with fear. It is questioned whether the group of symptoms attending angina pectoris should be dignified as a distinct disease, especially since the pathologic findings vary in different cases; yet the variation is much less than in many other affections recognized as morbid entities, so called.

Most authors also recognize pseudo, false or mock angina, which is of nervous origin and commonly associated with intercostal neuralgia. This is much more common in young people than in old, and more frequent in women than in men, although only three-fifths of my series of cases were in women, which is a much smaller proportion than I had supposed. It is not a serious affection, although the symptoms are not very different from those of true angina. A careful distinction must be made between these purely neurotic manifestations and mild attacks of true angina associated with diseases of the arteries or of the heart. The neurotic or vasovagal cases are not angina pectoris, although many cases commonly classified under this head are really true angina. Indeed, most cases of so-called pseudo-angina are manifestations of the true disease. Out of 60 cases I observed, 28 were classified as pseudo-angina and 32 as true angina; but in the absence of pathologic demonstrations I am inclined to think that in some of them my diagnosis was at fault and that they should have been classed as angina minor, that is, mild attacks of the true angina. Pseudo-angina thus appears to be much less frequent than was formerly supposed.

Many authorities recognize angina sine dolore, which is accompanied by paroxysms of cardiac dyspnea, and is usually quickly fatal, but not attended by pain, or at least, not by severe pain. This is quite different in its manifestations from the angina with which we are most familiar. It is considered by Balfour as one of the manifestations of true angina pectoris; and its frequent appearance in persons who at times suffer from severe paroxysms of cardiac pain with a sense of impending death, together with pathologic findings, support Balfour's view.

The commonly accepted views of the frequency, etiology and prognosis of pseudo-angina, true angina and angina sine dolore, I think, would be changed by a careful study of the evidence presented in this work. Such a study, I feel, would make clinicians more careful in their diagnosis and more helpful in their treatment of patients.

MORBID ANATOMY AND PATHOLOGY

True angina is generally supposed to depend on disease of the coronary arteries, causing their contraction or obliteration and thus interfering with the nutrition of the myocardium. But if, as held by some observers, it more commonly results from disease of the aorta or possibly of some of the other arteries, we can more readily understand the diverse seats of pain and we can better realize why very often the heart is not at all disturbed even by most severe attacks. Myocardial disease is not essential to angina pectoris, although it is present in many cases. It also seems proved that angina does not occur in the majority of cases of coronary occlusion.

As for the mechanism by which the pain is brought on, it is probably due to excitation of the nerve end organs in the sheath of the ascending aorta and other large arteries. It is the kind of pain that belongs to fibrous tissues.

PREDISPOSING CAUSES

In my series of 32 cases, 4 were under 30 years; 5 between 30 and 40; 6 between 40 and 50; 7 betwen 50 and 60; 7 between 60 and 70; 2 between 70 and 80, and 1 of more than 80 years. It is thus more common between the ages of 50 and 70. It is more common in men, as may be seen by my series which included 20 men and 11 women. The use of alcoholics, tobacco and coffee predisposes.

It is asserted that syphilis is a factor, especially in those under 45 years old. Typhoid, rheumatism, gout and influenza predispose in patients of more than 45. In some mild cases in which the patients seem to be benefited by exercise, it is probably of gouty origin. In those past 50 years of age, arteriosclerosis and high blood pressure, especially if associated with diseases of the aorta, are etiologic factors. It also occurs with mitral stenosis, thrombosis and pericarditis. Angina pectoris and aneurysm are often coincident, but the angina frequently appears a long time before the discovery of the aneurysm.

Occupation.—It is a curious fact that out of 32 cases classified as true angina pectoris, 9 were in physicians, or nearly 30 per cent. I saw two others that were not included in the list because they were not my patients. I attach no significance to these figures because I do not know why I was consulted by so many physicians; but they serve to emphasize the danger of drawing conclusions from incomplete statistics, and are at least suggestive as to syphilis as an etiologic factor.

EXCITING CAUSES

Some vasomotor disturbance, worry, muscular effort, or annoyance of any kind may bring on an attack. Pain frequently comes on during or after a meal, especially breakfast. Minor attacks of angina are brought on in the same way as the more severe. Only a few cases seem due to a single effort, but two of my cases certainly started in this way, and in X, whose history follows, the first distinct substernal pain was brought on by a rapid walk.

Among the various hypotheses regarding the origin of angina pectoris are distention of the ventricles, cramp of the heart muscle, myocardial ischemia, obstruction and spasm of the coronary arteries, and neuralgia, or vasomotor storm.

The coronary disease is considered a cause by most physicians, but it has been found that a large percentage of those with coronary obstruction have not suffered from angina pectoris. If the process is gradual, a patient may live with 75% of the coronary lumen occluded, or even with complete obliteration. The spasm hypothesis also seems untenable, though a sudden obstruction of the coronary arteries may cause pain like angina pectoris. In many cases, even though the coronaries may be obstructed, the myocardium remains practically normal. Blocking of the coronary arteries causes dyspnea but often no pain. In a large proportion of fatal cases of angina pectoris, no obstruction of the coronaries is found; but in most fatal cases there is some change in the coronary arteries and myocardial degeneration. These changes, however, are not the cause of the pain, but are one of the chief factors of death during the disease. Often the rhythm of the heart is unchanged and the blood pressure is not affected by the painful attacks.

As to the immediate cause of the pain, there are convincing arguments to show that it is not due to cramp of the heart, to distention of the left ventricle, or to undue systolic effort. The experience of X leads me to coincide fully with these views. The pains seem to result from an exalted state of the sensory paths, which appear to be along the aorta and larger arteries. Arteries, whether inflamed or not, are capable of pain, as shown in embolism and on compression for aneurysms, and angina is usually the result of inflammation in the aorta and larger arteries. From his own sensation, X feels that much of his pain comes from this source, as indicated by the sudden feeling of distention and by the location of the pain. The suprasigmoid portion of the aorta is probably the most sensitive, angina resulting when

the fibrous outer investment is reached. The fact that the use of iodids sometimes stops the horrible pain of aneurysm, and also often stops pain in angina, indicates that the pain in these two affections may be due to the same cause. Tension of fibrous structures in any part of the body may cause pain, and this tension is the principal factor in angina pectoris. At the base of the heart there is most likely a point of exalted sensibility to blood pressure. Perhaps all arteries have their degrees of sensibility to blood pressure.

If, as maintained by some, the disease results from an affection of the coronary arteries with degeneration of the myocardium, it is difficult to understand why the heart's action is commonly almost normal, and why the pain usually referred to the precordial region is commonly felt over the aorta and radiates along the course of the larger arteries. The theory that the real seat of the disease is usually in the arterial walls and often in the external coat accounts for the incidence of the pain much better than the older theory.

SYMPTOMATOLOGY

The physical signs are not characteristic, but often there is moderate enlargement of the aorta and enlargement of the heart in many cases. There may be an aortic murmur and the rhythm of the heart may be affected, but all these symptoms may be absent.

The blood pressure may be excessive, but usually it is not affected. The pulse commonly remains nearly normal, but often, although regular, it may run as low as 40 or 50, and it has been observed as low as 21 per minute. I recall 3 cases of abnormally slow pulse seen at nearly the same time with nothing in common but the pain.

Profuse sweating is not an uncommon symptom, and salivation occasionally occurs.

Fever may sometimes be present from the acute aortitis. The face may be pale, flushed or normal.

There may be restlessness and tremors.

Flatulence and gaseous eructations are generally present.

Dyspnea is not a characteristic feature, but when the heart muscle is weak, it is likely to be present.

The pain in angina is usually paroxysmal, rarely a steady grind. It may increase from slight to extreme anguish. It may be short and sharp for an instant only, but it usually lasts from several minutes to half an hour or more, and occasionally continues much of the time for days. Sometimes it is confined to the chest; at other times it

radiates to one or the other arm, rarely to the thigh. It is located sometimes in the neck and occasionally in the throat or larynx. It is sometimes felt on the radial side of the arms and may run down to the thumb. In some erratic cases, the pain may be confined to the periphery, as to the palm of the hand, or to a finger, and in one of my cases it was often felt in the rim of the ears. It may also be felt in the epigastrium, the apex of the heart or the abdomen. There are some cases in which the patient has a horror but an absence of pain. Angina without pain (angina sine dolore) is comparatively rare, but may be the cause of death in many of those who die suddenly without symptoms.

The heart pain in angina pectoris is usually said to be precordial; but in reality it is nearly always felt at the upper part of the sternum over the aorta. In one case that I have observed, it started in the region of the left subclavian and was so constant that the patient, a physician, believed there was an aneurysm of this artery. With X it usually started over the brachial artery in the middle of the right arm.

When the aorta is the seat of the lesion, the pain on exertion is likely to radiate to the shoulders, and it generally extends down the left arm, the reason for which proceeding is not apparent. It is sometimes relieved by eructations of gas, and such cases are very likely to be attributed to indigestion. In a few instances paresthesia or even paralysis of the arm follows the attack.

Immobility from a fear to move, or a feeling that one cannot move, is a common symptom. The feeling of impending death or of horror is not a reasonable apprehension, nor a fright, but an organic sensation, a feeling as though everything was going and nothing mattered. It may occur in only one or a few of the attacks, and sometimes is altogether absent.

The history of a single case illustrates most of the features of this disease so well that I will present it briefly at this point.

REPORT OF CASE

When 63 years of age, Dr. X suffered a comparatively mild attack of typhoid fever in which the temperature never exceeded 103.5 F. He was not delirious, lost only about 30 lbs. in weight, and was confined to his home only 3 months. He had suffered from no infection nor sickness of any kind for forty years, although since boyhood he had often had rheumatic pains on exposure, and for about 15 years had gouty pains with enlargements of the joints in one finger after another, each joint remaining tender for about 18 months. This was a hereditary condition. His parents lived well on into the eighties, and of 5 brothers and sisters of which he was one, all are still living, the youngest

being 55 and the oldest 72 years of age; and all are well except for a chronic gouty condition of the fingers.

Three or four days after leaving his room, he was able to go to his office for an hour daily. For several months he was troubled a good deal with dyspnea, on walking or attempting to carry even light weights. Gradually he regained strength and experienced no pain in the chest until after a brisk walk of about 500 yards in the autumn when he was 64 years of age. When he rested a little and walked slowly this pain subsided, but did not disappear for about 20 minutes. For several years he suffered frequent pains at the middle of the arms directly over the brachial artery, usually on the right side, and occasionally an aching pain in the elbow. The one in the right arm was especially severe sometimes shortly after breakfast or after exercise. These pains he attributed to rheumatism, as they usually occurred with changing weather or whenever he was chilled. He worked hard, but was very temperate in his habits, using no alcoholics, tobacco or coffee, and very little tea. His appetite and digestion were good, and he regulated the amount he ate so as to keep his weight down to the average for his size. He had no pain that he recognized as angina pectoris until the middle of May, 1913, when 64 years of age. For a few days he had found himself getting out of breath easily, and one night while in bed he had a distinct attack of angina pectoris, though not severe enough so that he called any one.

After this, the pain over the aorta came with increasing frequency and severity, so that within a couple of weeks he decided to go to Nauheim, Germany. But while waiting for a steamer he went daily to his office, where he lay on a couch most of the time directing the work of his assistants, unable to walk more than 4 or 5 paces without bringing on the pain. During these 4 weeks he at times took aspirin to relieve the pain, and several times tried nitroglycerin, but without any relief, probably on account of the fact that the preparation was too old. He also tried amyl nitrite, but without much satisfaction. He took no opiates, as they always disturbed his digestion.

He arrived at Nauheim very weak and unable to walk for more than a few yards without pain. There he took the regular cure of baths, went about all the time for 6 weeks in a wheel chair, rested 1½ hours or more every day, and had gentle massage of evenings. He felt so cold most of the time that he wore a heavy ulster and was wrapped in blankets all summer long, whenever he was outdoors. After his 6 weeks' course of treatment, he could walk slowly about 50 feet before the pain would compel him to stop, and after a few minutes could repeat the exertion. He gradually regained strength, so that on his return in the fall he could walk slowly for from 50 to 75 yards on a level, according to the weather, the temperature, etc. A few months later he discovered that fresh hypodermic tablets of nitroglycerin dissolved on the tongue would relieve the pain in 2 or 3 minutes, although they might cause dizziness and headache. The same tablets swallowed would not give relief for about 10 minutes, and then only about half as much as when dissolved in the mouth. As sodium nitrite and erythrol tetranitrate quickly caused disturbance of his stomach, they could not be taken. At Nauheim he was advised to take theobromin, 15 grains, 3 times a day; but as he was very sensitive to all medicines, he took only 5-grain doses, and this only 5 or 6 times, as it greatly increased the heart pulsations and intermissions. Caffein appeared to make him worse. Strychnin or nux vomica kept him awake, and doses of digitalis sufficient to reduce the pulse to normal seemed to make his pains worse after a short time.

During this period the heart intermitted several times a minute, and the pulse usually ran from 85 to 120. The blood pressure was about 130 to 140 and never was found more than 148.

In the beginning of the disease, X, judging from the suddenness and location of the pain and from the feeling of distention, felt that the trouble must be in the arteries, although he found no confirmation of this theory until he read Allbutt's work four years later. Allbutt argues that pressure on an artery, as in treating aneurysm or an embolus, causes acute pain. X found that after sleeping for an hour or two on the right side he would sometimes waken with acute pain in the right arm, which would quickly be relieved by his taking nitroglycerin. This seems to support the arterial theory, for there had been nothing during this sleep to disturb the heart except the weight of the body pressing on the right arm. The excessive fatigue which he experienced at times, however, even with no unusual exertion, points sharply to myocardial degeneration.

As the anginous pains came just as the thumb joints were recovering, he suspected that they were of gouty origin, and therefore, for about 2 years, gave up the use of meat almost completely. Frequent experiments convinced him that the white meat of fowl was to him as injurious as beefsteak or roast beef. Later, on account of the weak myocardium, he returned to the use of meat in moderation.

The pains in this case were brought on by a variety of conditions, such as walking at an ordinary gait on a level, climbing a very slight grade, going up 4 or 5 steps, or feeling moderate excitement, pleasurable, or more particularly annoying. A moderately full meal or the act of putting on his shoes after eating, or even of brushing his teeth, or of reaching up to take down his overcoat, or of being in the slightest hurry were all followed by pain.

The sufferer from repeated attacks of angina is usually worse in cold or stormy weather. The latter is not necessarily the result of chilling, for it may and often does occur while the patient is in bed in a warm room. It is apparently due to the subtle meteorological conditions heralded by the pains in chronic rheumatism for hours before an approaching storm.

In the case of X, attacks were brought on by a chilling of the surface, by even slight changes of weather, and once by a wind storm that he encountered when traveling in a warm car. During the blizzard early in January, 1918, X suffered continually for about 48 hours with severe angina pains in or under the lower part of the sternum, and in the stomach and arms, when he was not under the influence of large and frequently repeated doses of nitroglycerin. The remedy seemed to be losing its effects, but these pains finally subsided under the influence of heat applied by means of an electric pad, which was kept hot for about 12 hours. During this time, it was sometimes necessary for him to take 3 or 4 doses of the nitroglycerin in the course of 15 minutes, in order to be able to eat even a very light meal. The pain did not return with any severity for several weeks. It often came on while he was eating or addressing a company of his fellows. Indeed, almost anything that increased the rate of the pulse for a few seconds seemed sufficient to cause the pain in the arms or through the shoulders. The same exciting factor carried a trifle further brought the pain over the aorta, or if carried still further, brought on that awful horror which is spoken of as the sense of impending death.

During the pain, even though it was not very severe, he was afraid to move lest it be greatly increased, and once although the nitroglycerin was only 4 or 5 feet away, he hesitated some minutes before he could nerve himself to get it. He carried the tablets in a closely stoppered half-dram bottle in the pockets of every suit, and always had a bottle within easy reach of his bed.

By riding a light motor wheel, he was able to play golf during part of each of the last 3 summers; but on the days he played, he had to take from ten to twelve 1/100 grain tablets in the course of a couple of hours. He found that frequently on the day after playing, he had no pain, whereas usually he had it several times a day.

In 2 years, he took 3 courses of saline baths of the same content as the bath most used at Nauheim. The most important feature of his treatment was an afternoon rest in bed for about 2 hours daily with from 8 to 9 hours' rest at night, his daily work being limited to 5 or 6 hours. After the trial of many medicines, he settled down to nitroglycerin as often as needed, taking usually 4-10 doses a day, and twice daily arsenous oxid, 1/24 grain with extract of digitalis, 1/4 grain, extract of nuxvomica, 1/4 grain, and 1 1/8 grains of chlorbutanol to prevent insomnia. On this plan he has been able to continue his work in the past 2 years. He feels the pain often and has to take rather more of the nitroglycerin than formerly, but thus far he has found that it relieves the pain very soon if used in sufficient quantities. Recently, apparently on account of an unusual strain for a few seconds, the heart compensation broke, and he was obliged to take a prolonged rest. In spite of the rest, the pains have increased in frequency.[1]

DIAGNOSIS

The diagnosis is usually based on substernal pain radiating to the arm, shoulders or neck, accompanied by a peculiar mental depression or a sense of impending death, aggravated by exertion or even by slight movements; but it may come on, as in the case of X, even during sleep. We should always suspect angina pectoris when pains result from exertion, no matter what their seat, especially in the aged or the syphilitic. The pain is often attributed to indigestion, but we must be suspicious if it is excited by exertion. I have known several men about 65 years old who, while apparently in excellent health, have been suddenly attacked with what the first physician to arrive termed acute indigestion; yet within a few minutes or at most a few hours, they were dead of angina pectoris. I have observed similar cases in which life has been saved by prompt and judicious treatment. When physicians realize that the pain of angina is seldom in the heart as usually described, but that it is commonly under the sternum or along the course of the larger arteries, so that it may even be in the stomach or bowels or other remote parts of the body, such errors and catastrophes will be much less frequent. If we have been taught to expect pain

[1] The weakness increased, edema developed and death occurred in an anginal attack in May, 1918. For report of the postmortem examination by Dr. E. R. Le Count see page 77.

only over the precordia and down the left arm, we are apt to miss the significance of a pain over the upper part of the sternum and in the right arm, and we are much more liable not to recognize the disease when the pain happens to be centered in the epigastrium or even over the lower part of the abdomen.

The relief of pains by nitrites is considered a diagnostic feature; but this is not necessarily the case, for the nitrites do not always give relief, even under the best conditions. It must also be remembered that the nitrites are not effective when the preparation is old. The pains of pseudo-angina are relieved by the nitrites, and it is probable that still other pains may be relieved by these remedies, just as bronchial asthma is often promptly relieved.

It is asserted that angina pectoris in persons under 45 is usually of syphilitic origin. Possibly this is the explanation for the benefit that has sometimes been obtained from arsenic and the iodids. The value of a syphilitic history as a diagnostic point, however, cannot generally be relied on, as very few private patients will admit that they have had the disease if they can avoid the admission.

In pseudo-angina, the symptoms are much like those of the real disease; but the jactitation and absence of that awful feeling of impending death (I do not mean fear of death), together with the history and the position of the pain, usually make a diagnosis reasonably certain. I think that with many of us the crucial test has been found in the result. We have been accustomed to consider that the patient who recovered had an attack of pseudo-angina, whereas we are ready to admit that the one who died had the real thing.

PROGNOSIS

In the milder forms of the disease, suitable care and treatment may prolong life possibly for many years. For myself I know that I had come to think that with real angina pectoris, the first, second or third attack was almost sure to be fatal; but a careful analysis of my own 60 private cases and especially the experience of X, who, several times a day for 4½ years, has suffered more or less severe attacks, many of which might have been serious but for the means of prompt relief, have greatly modified this view. I unfortunately have not the end-results in many of my cases; but of the 28 cases that I classified as pseudo-angina, 3 patients had already lived 4 years when my last notes were entered. Of the 31 cases in which I had no doubt about the reality of the disease, 2 patients had lived from one to two years; 3,

two years; 4, three years; 4, from three to four years; 1, five years; 1, eight years; 1, twelve years; 1, fifteen years, and 1, thirty years. This would seem to indicate that those with true angina had outlived the pseudo-angina; but as I have records of death in only 4 cases with true angina and none in pseudo-angina, the figures have no significance as to end-results. They do show, however, that true angina is not nearly as hopeless as we are wont to believe, and that not a few may live to comparatively old age.

Allbutt makes a more hopeful prognosis than most authorities. This should be comforting to those who have experienced the pains and the awful mental depression that accompanies them. He thinks there is no close relation between the danger and the severity of the pain, but the degree of "angor" is the most ominous symptom. Without angor, angina minor many last for years or may even disappear. One of our fellows who had the pains often a few years ago is now quite free of them, although not young, and is very active in his profession. I have seen cases that lasted more than 10 years, and I knew intimately one woman who suffered for 30 years, having at times very severe attacks. The celebrated John Hunter suffered from angina pectoris for 20 years before he finally died in an attack. During the 4 years, X has improved much in some respects, and if he can maintain a corresponding rate of gain for the next 15 or 20 years, he hopes to be well.

In the majority of fatal cases, death is due to inhibition of the vagus, stung by pain. A fall in blood pressure resulting from mitral disease or from administration of nitrites relieves the vagus and saves life. An aortic murmur in syphilitic cases is of grave importance, indicating rapidly progressing changes. There are no physical signs that aid much in determining the probable duration, except that weakness of the heart sounds is indicative of myocardial changes, which add greatly to the danger. A sound heart can free itself from vagus arrest, but an enfeebled heart may fail. Chronic aortitis may suddenly end in angina pectoris.

TREATMENT

Nitrites are among the most valuable remedies, but they are commonly given in insufficient doses. X found the most satisfactory preparation a hypodermic tablet of nitroglycerin of $1/100$ grain, which was found to act more promptly and effectively than otherwise, when allowed to dissolve on or beneath the tongue. In this way its full effects were experienced in from 1-3 minutes, whereas, if it had been

taken into the stomach, only about half the efficiency was experienced, and it did not appear for about 10 minutes. Frequently 2 or more of these tablets were taken at once, and they were repeated every few minutes until the desired effect was obtained. Often as many as 10 or a dozen were taken in 2 or 3 hours. As much as 15 to 20 hundredths of a grain 3 times a day has been recommended in severe cases. A physician told me of one patient who took 100 of the $\frac{1}{100}$ grain nitroglycerin tablets in 1 day with the effect of relieving a severe angina, and at that time he said the pain had not returned for 3 years. X usually took 4 or 5 of the tablets daily, and when the pain was worse or more persistent, 10 or 12. Frequently after these larger doses he would be entirely free from pain all the next day. From my personal observation, I think these large doses are often needed; and if the physician feels his way with gradually increasing doses, no harm will come from them unless they cause too much headache. Osler thinks nitroglycerin is too timidly used and is then abandoned as ineffective. The preparation should be reasonably fresh, and prescribed in the original package. It may be carried in a small closely stoppered bottle to prevent evaporation, and renewed from the original package every week or two. The patient should be warned of the possible dizziness, the flushing of the face and the headache resulting from its use, and should be assured that these disorders will do no harm. I have found it a good plan to give the patient $\frac{1}{100}$ grain or more at once, so as to learn its effects before he leaves my office. After the susceptibility has been determined, it is best to give a full dose when attacks come on. It may be repeated as often as necessary to accomplish the result, except when it causes too much headache. The headache is sometimes relieved by repeating the dose. This remedy does no harm even from prolonged use. It is of doubtful utility when given only three times a day in the conventional dose of $\frac{1}{100}$ grain.

X did not like amyl nitrite because of its odor, and also because during an attack he found it difficult to dispose of the glass. It is asserted that although this remedy acts quickly it is not as certain as nitroglycerin. The few times that X used it, its effects were practically nil.

Sodium nitrite disturbed his stomach, by the time 2 or 3 doses had been taken. This drug seems to have some toxic property. Erythrol tetranitrate caused more headache and did not relieve the pain as

promptly as the nitroglycerin, although some patients have found it more satisfactory because of longer duration of its effects.

The heart may be protected against inhibition shock by more or less continuous use of atropin. The dose employed is often too small. As much as 2 mg. or $\frac{3}{100}$ grain may be needed with some adults. In cases of extremely slow pulse, atropin has quickly relieved the inhibition. Calcium lactate is mentioned by some authors as a possible aid to check inhibition.

It is important to inquire into the cause; and if there has been syphilis, the proper treatment should be adopted, as potassium iodid and the arsenical preparations. Arsenic has been used since 1879, and is recommended in small or large doses to forestall the pain. The prolonged use of potassium iodid is said by some to be very effective. I myself have not seen much benefit from these remedies; but in view of the contention that nearly all cases of angina pectoris in persons less than 45 years old are syphilitic, it is possible that many of them might be benefited by these remedies.

During the attack, if prolonged and severe, morphin, or morphin and atropin, given together hypodermically, are the most common remedies. They are undoubtedly necessary in many cases, but they usually disturb the digestion and make the patient feel bad for two or three days, so that it is much better to give the nitrites first and rely on them when they will answer the purpose. Whisky in quantities of about 3 ounces will also give relief. Hot applications over the sternum, as an electric pad, are sometimes helpful in relieving pain. Balfour recommended chloroform to be inhaled from a wide-mouthed bottle in which about a dram had been placed on a sponge. The bottle was to be held in the patient's hand so that, as he came under the influence of the anesthetic, the bottle would drop and roll away. Allbutt considers chloroform dangerous. I do not know its value from personal experience in angina pectoris, but have found this method of administration very effective and safe in some other painful conditions.

On account of its reputed effect in contracting the arterioles, digitalis is not suited to relieve an acute attack. In those cases in which the heart's action remains practically normal, it is distinctly contraindicated. When the heart's action is feeble, however, this remedy and nux vomica are indicated. The two together will often yield results that cannot be obtained by either one given alone. X tried

digitalis repeatedly, but became convinced that at times it made him worse, although he never had high blood pressure. In 60 cases I observed, in which the condition of the heart and pulse was recorded, the heart was apparently normal in 36 cases, and the pulse did not exceed 85 in 26 cases. In only 11 cases did the myocardium or valves appear to be involved, in only 19 did the pulse run from 85 to 90, and in only 12 did it run higher than 90 at the time of my examination.

To prevent the attacks, it is of first importance that the patient live a regular life, and avoid over-exertion, mental excitement, chilling of the surface and, indeed, anything that brings on the pain.

Moderation in eating should be enjoined, especially on those who are overweight, and mild measures for reducing the obesity should be instituted. Tobacco, coffee and sometimes tea should be avoided. Flatulence should be relieved by such remedies as rhubarb, gentian, and the carminatives, as peppermint, cardamom and ginger. The Bacillus bulgaricus has been quite effective in preventing flatulence in some persons. The secretions must be free and the bowels must be kept open.

Rest, especially in the early stages or when the attacks recur frequently, is of the utmost importance; but the patient's temperament must be considered, and the physician must not demand what to the patient seems impossible. I am impressed with the idea that rest and diversion with graduated exercise are the greatest factors in the beneficent effects of baths of the type given at Nauheim. Essentially the same baths may be given at home, by adding 9 pounds of sea salt and 10 ounces of commercial calcium chlorid to 40 gallons of water with or without carbonic acid gas. Calcium chlorid is probably the most essential ingredient. The carbonic acid gas appears to me negligible except for its psychic effect. As already pointed out, X improved markedly during his 6 weeks of treatment at Nauheim, and has continued to improve since. This case yields a hopeful aspect in prognosis and, I think, illustrates some important facts in treatment, the outstanding features of which are avoidance of exciting causes, heart tonics when needed, nitrites given freely to relieve pain, regular temperate habits, and abundant rest. I believe his improvement is due first to the free use of nitroglycerin, partly to the heart tonics he has taken almost continuously, partly to the care in diet, and largely to the 1½ or 2 hours' rest every afternoon, added to the 8 hours at night.

SUMMARY

The pain in angina pectoris is not usually in the heart and the left arm, but rather along the course of the aorta and large arteries.

The pain appears, at least in many cases, to have no relation to the condition of the myocardium or to the obstruction of the coronary arteries.

A more hopeful prognosis than that of the usual conception of this disease may be assured under proper care and treatment, a very important part of which is abundant rest with heart tonics as needed.

The sublingual administration of fresh hypodermic tablets of nitroglycerin in large amounts to relieve pain is of great value. The failure of nitroglycerin is most often due to the wrong mode of administration, deterioration of the preparation, and inadequacy of the amount.

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PATHOLOGY OF ANGINA PECTORIS

E. R. LeCount

March 28, 1918

When sudden occlusion takes place in an artery supplying blood to a place which no other artery can adequately supply, because anastomosis with neighboring arteries is not sufficient, the process is called infarction and the name is generally applied also to the changes which result in the region having its blood supply so interfered with; the lesion produced is an infarct.

There are very few if any arteries which in a strict sense are terminal, that is to say, so terminal that the entire tissue supplied by them must of necessity die when their circulation is obstructed.

Many so-called terminal arteries are so in only a small degree, which means that only part of the region they supply undergoes death by anemic necrosis when they are abruptly occluded. Indeed, the existence of so many different degrees of terminality, if such an expression is allowable, has resulted in a great deal of contention between those who have maintained that arteries for some part of the human body are "end" vessels, and others who with equal vigor have insisted that they are not. Naturally these differences of view have led to experiments of one sort or another, to estimate in some precise way the extent to which the normal circulation in some of these terminal arteries is essential to the healthy life of the region supplied.

Unfortunately for many of these experiments, lower animals have been used; and the conditions, for some organs at least, only approximate those in the corresponding human organ.

Exception may be taken also to the conclusions founded on conditions ascertained by anatomic studies, the injection of arteries supposed to be terminal to ascertain the extent such injection-masses may be made to penetrate the capillary bed and larger branches of neighbor-arteries; for, valuable as these studies are, they do not measure the functional compensation possible by means of such anatomically demonstrable collateral anastomosis; in other words, proof by such methods of collateral communication is not a measure of the degree to which the vessels in question are functionally terminal.

The coronary arteries are virtually the sole route by which arterial blood is supplied to the heart. Because they possess some collateral

circulation, and also of course because the maintenance of an adequate supply of blood by these arteries is necessary for life to continue, the amount of such collateral circulation in the human heart, and especially its ability to functionate in a compensatory way, has been subjected to extensive study.

Reference has been made thus far only to sudden occlusion; and it is worthy of comment at this time that experiments with the coronary arteries have practically all dealt with the consequences of obstructing the circulation in one or both of these vessels or their branches, by methods which have abruptly interfered with the circulation.

The relation impaired circulation in the coronary arteries is supposed to have to angina pectoris is, however, not limited to simply sudden or acute obstruction, but is believed to apply equally well to a gradual hindrance extending at times over many years.

It is generally believed that somewhere between sudden occlusion and its results, and such slowly developing obstruction that few or no symptoms develop, lie the lesions responsible for angina pectoris; and because of this I propose to discuss briefly such details as I possess regarding 60 deaths from difficulties with the circulation of blood in the coronary arteries or with lesions generally regarded as caused by such difficulty. These are in 2 groups: 34 deaths from fibrous myocarditis with sclerosis of the coronary arteries, and 26 of more or less acute occlusion.

FIBROUS MYOCARDITIS

Only 4 of 34 persons whose deaths from the postmortem examination were found to be due to fibrous myocarditis were in a hospital for any time and ill from heart disease; one for 8 hours, with a clinical diagnosis of acute dilatation of the heart; one for 8.50 hours, with a diagnosis of pulmonary tuberculosis; a third, 17.40 hours, with a diagnosis of asthma, and the fourth for 27.50 hours, with a diagnosis of delirium tremens.

Twenty-eight of these 34 patients were men and 6 were women. Three under treatment for other illness and convalescent died suddenly and unexpectedly, 8 died en route to the hospital, and 18 were found dead; and of these last, 4 fell dead on the street and 7 were found dead in bed.

In five of the 34 hearts the scars were of such size in the heart muscle that pouching outward had taken place—the so-called chronic parietal aneurysms. In a few the scars replaced so little of the myocardium that, in addition to other examinations, a chemical examina-

tion was made for poisons. In 4 of the 34 bodies, gross indications of syphilis were present, in 4 others there was pulmonary emphysema of the hypertrophic variety, in 2 the kidneys were markedly diseased — "small red granular kidneys." There was some anasarca or hydrops or both in 8 of the 34, obesity in 1, and 2 hearts possessed anomalies, a two-cusped aortic outlet in 1 and absence of a circumflex branch of the right coronary artery in the other, the corresponding branch of the left coronary being large.

Four of the 34 patients were between 30 and 40 years old, 8 between 40 and 50, 13 between 50 and 60, 6 between 60 and 70, and 1 over 80 years. It will be noted that the decade for the greatest number was between 50 and 60.

One man, a pedler, aged about 60, came into a saloon and said he wished to rest, and later was found dead in the back room on a couch where he had lain down. The man in the hospital for 8.50 hours said he had been ill for 3 days, unable to retain anything on his stomach, but also unable to attribute this to any indiscretion in diet. Another was under treatment in the hospital for urethral stricture, went to the toilet, and on returning dropped dead at the bedside.

Another found sick on the street by a policeman died soon after being taken into a barber shop. Another dropped dead shoveling sand; one died suddenly in a police cell; one of the 6 women dropped dead when prepared to leave her work in the Psychopathic Hospital, where she worked nights; she had just dressed to leave. Another woman fell dead on the street, and a third woman died suddenly in a drugstore.

ACUTE CORONARY OBSTRUCTION

Of 26 persons who died with acute or suddenly developing obstruction of the coronary arteries, 18 were men and 8 women. Of these the age of the greatest number in any single period of 10 years is 2 decades earlier than those with the fibrous myocarditis, one being in the 20 to 30 decade, eight between 30 and 40, six between 40 and 50, six also between 50 and 60, three between 60 and 70, and two 71 years old or over. This earlier age for the largest number in any one decade is no doubt connected with syphilis, for in 11 of the 26 bodies, changes usually regarded as indicative of syphilis were found, whereas with the 34 deaths from fibrous myocarditis, only 4 were of persons whose bodies possessed such alterations. Of the 26 patients, 5 died in the examining room, 5 were found dead, and 1 died en route to the hospital.

The obstruction of the coronary circulation of these 26 persons was in most instances thrombosis; in one instance embolism was associated with thrombo-ulcerative mitral endocarditis, and embolic hemorrhages were present in the skin and bowel as well. In another heart acute dissection of the wall of the circumflex branch of the left coronary artery was associated with a minute sacculated aneurysm at the same place. In a third the coronary artery broke open and the blood from it found at the postmortem examination in the pericardial sac weighed 560 gm. In 4 others, syphilis of the root of the aorta had obstructed the coronary circulation at the mouths of the arteries. One of these was interesting in that a small globular clot formed where the intima of the aortic root was altered from syphilis, had obstructed the mouth of the left coronary artery completely. Another concerned a pregnant housewife only 21 years of age.

In another heart the obstruction was apparently due to calcareous masses which were partly loosened in the channel by softening of patches of atheroma of which they were a part. This man, aged 60, had become acutely ill, and was on his way to the hospital without aid. He had almost arrived when overcome. He died in the examining room. In addition to the obstruction with loose lime masses and the infarction of the myocardium, the anterior papillary muscle was found greatly atrophied and shrunken, there was some fibrous myocarditis, and the heart weighed 455 gm.

Mention has been made of a small saccular aneurysm of the branch of the left coronary artery, which runs around the heart referred to here as the circumflex branch, and its association with acute dissection of the artery wall at the same site. In two other hearts the obstruction was similarly located, once in the left circumflex branch and once in the right.

The regions of infarction in these hearts were for the most part large and easily found; many were, as is commonly known to be the case, considerable distances away from the place where the artery was occluded or the circulation otherwise interfered with. Infarcts of the myocardium are frequently multiple, and sometimes small and widely scattered.

In 1 of these 26 hearts the place softened by anemic necrosis broke so that the pericardial sac filled with blood; in several, acute outpouching in varying degrees was present; in many, mural thrombi had formed on the necrotic lining. Small, delicate deposits of fibrin on or in the epicardium of the place infarcted was not uncommon.

These 26 deaths from more or less acute obstruction of the coronary circulation are the only ones of 175 deaths from heart disease with which I have found associated symptoms suggestive of angina pectoris.[1] Fifteen of the 26 were patients for a short time. The shortest period under observation was 1.15 hours, and the longest, 52.20 hours.

The diagnoses made in these short periods are of interest. Twice the diagnosis of angina pectoris was made; for 2 others, acute dilatation of the heart; for 1, edema of the lungs; for 2, lobar pneumonia; and once each, pulmonary tuberculosis, acute gastritis, intestinal obstruction and carcinoma of the stomach.

One of these acute coronary obstructions had to do with the heart of a man found dead seated in a chair. He had been ill two months and under the care of a surgeon well known to us all whose diagnosis of gallstones I have in a letter in answer to one of inquiry sent him. I found no gallstones, and there had been no operation. The following are brief synopses of single cases:

Time under observation, 26.10 hours. An elevator man, aged 61. Illness began 5 days before entrance with a sudden pain in the chest which spread to each side and was increased by deep inspiration. There was vomiting at intervals during these 5 days.

Time under observation, 16.20 hours. Age, 30; Italian. Three days before death there was pain in the lower chest and abdomen with vomiting. The respirations were from 32 to 40. The pulse was too fast to count. The clinical diagnosis was lobar pneumonia.

Time under observation, 52.20 hours. A German woman, aged 43, a nurse. Illness began 2½ days before death with pain of the back of the neck, front of the neck and across the chest pronounced neuralgia by one physician, and heart disease by another. In the hospital the pain was all on the left side and involved the neck, both extremities and the left side of the chest. The clinical diagnosis was angina pectoris.

Time under observation, 28.15 hours. Woman, aged 50, housewife. Illness began 5 days before with vomiting 1½ hours after eating a heavy meal, and severe cramp-like pains of the epigastrium persisting during the 5 days.

Time under observation, 8.30 hours. Man, aged 35, became ill 22 days before death after working 14 hours without food in a brickyard, with pain in the chest and shortness of breath, and vomiting for several days shortly after eating. When in the hospital he did not have much pain, but spat up a blood-stained froth and was very cyanotic. The clinical diagnosis was edema of the lungs.

Time in the hospital, 20.15 hours. Man, aged 53, telegraph operator. While walking 2 weeks before death his illness began suddenly with a severe pain in the chest, and he was obliged to stand still or lean against something for support and gasp for breath. This lasted only a few minutes, but was repeated

[1] These 175 necropsies were all medico-legal, a part of inquiries necessary because the deaths were unexpected, or because of an absence of medical attention sufficient to ascertain the nature of the illness.

3 or 4 times in walking a block. Four days before coming to the hospital he had a similar attack in bed, and a physician came and gave him a hypodermic and he had suffered but little pain since; but the shortness of breath persisted and remained worse on slight exertion during all the two weeks. The clinical diagnosis was angina pectoris.

COMMENT

It may be assumed that none of these 60 persons suffered from angina pectoris, that there are no reliable accounts of the angor said to be associated with a sense of impending death or that many were examples of pseudo or mock angina. I have no answer to such assertions unless it be to state that in all likelihood many die from true angina in a first attack and that some people with true angina suffer as others do but without any realization that death is at hand; no doubt people vary as to their ability to discriminate with regard to the likelihood of death ending their distress and with regard to their fear of death.

As to the contention by Allbutt that the lesions are not located in the coronary arteries but in either functional or structural alterations of the aorta, I may remind you that anatomists have always debated somewhat as to where the heart ends and the aorta begins, where the boundary line between them lies.

Since the lower part of the aorta as well as of the pulmonary artery receives its blood supply from small branches of the coronary arteries, which, passing up, anastomose with similar vasa vasorum from the bronchial and pericardial arteries, it perhaps may be best to regard the proximal few cm. of both of these large arterial trunks as a portion of the heart.

It is not unlikely that with sclerosis of the coronary arteries a difficulty exists in maintaining an adequate supply of arterial blood to the proximal parts of these arteries, a difficulty which is concerned with insufficient anastomosis with the other vasa vasorum which come down from the bronchial and pericardial arteries; indeed, these last vessels may also be the seat of sclerosis.

With these conditions in mind, it is easy to conceive of these branches of the coronary arteries which supply arterial blood to the roots of the pulmonary artery and aorta as end arteries in much the same way as their chief branches to the myocardium are terminal, and to remember that, although a collateral anastomosis exists in the heart between the two coronary arteries and also between the coronary vasa vasorum of the aorta and other vasa vasorum to the aorta from the pericardial and bronchial arteries, with sclerosis or with more acutely

developing obstruction from other causes, the compensatory circulation may prove inadequate or may not be promptly enough established to prevent either angina pectoris with death, or death so unexpectedly that there is no opportunity to determine whether symptoms of angina did or did not occur.

DISCUSSION

DR. JAMES B. HERRICK: I wish to discuss four propositions: 1. Coronary thrombosis causes some attacks of angina. 2. Coronary thrombosis is not necessarily always fatal. 3. Coronary thrombosis produces a group of clinical symptoms that can frequently be recognized with a reasonable degree of certainty. 4. Experimental work seems to show that the electrocardiograph may be helpful in recognizing this condition. In speaking of coronary thrombosis we should also include some cases of coronary embolism.

As to the first proposition there is little need for discussion. All clinicians, I am sure, have seen cases of angina, which, if they have been checked by necropsy, have shown obstruction of the coronary artery by a thrombus.

The second proposition, that coronary thrombosis is not always necessarily fatal, is one that is perhaps today believed by most clinicians. Yet for many years the doctrine prevailed that the coronary arteries were terminal arteries and that their obstruction by thrombi was necessarily fatal. It has prevailed from the time of Parry, and John Hunter's celebrated case up to a few decades ago. It was fortified especially by the teachings of Cohnheim, who from his experience as a pathologist, and as the result of his experiments on dogs, said that obstruction of the coronary arteries was always followed by death in two minutes; but Cohnheim's dictum was soon challenged both as to the necessarily fatal result of obstruction of the coronary, and that the coronaries were end arteries. Dr. LeCount has spoken on this point.

The proof that these arteries are not end arteries comes from anatomists, pathologists, experimental workers and clinicians. Anatomists proved by dissections that there were anastomoses, not negligible, not merely capillary, but sometimes visible to the naked eye, between the right and the left coronary. This was proved by various other means of examination—by Spalteholz by rendering the heart translucent, by roentgenograms of injected vessels, etc. The pathologists have seen many cases in which, as we have heard tonight, the obstruction has clearly been of long standing, a condition that could not obtain unless there were a reasonable degree of blood supply from some other source than the one coronary artery. Later experimenters have had more favorable results than Cohnheim. A few weeks ago we heard Prof. W. T. Porter of Harvard speak of his experience in Europe. Porter was one of the first who was successful in having his animals live after ligation of large coronary vessels. Our colleague, Dr. Joseph L. Miller, with S. A. Matthews, also was successful, so that now it is not uncommon for experimenters to ligate large branches of the coronary artery and have the animals live for hours, days, weeks and months. This means that the coronaries are not, in the strict sense, terminal arteries.

Clinicians have seen patients, with symptoms that perhaps necropsy would show were clearly due to obstruction of the coronary, who have lived for hours, days, weeks or months. The point, therefore, that I wish to bring out is that obstruction of the coronary artery, even of a main branch, is not neces-

sarily fatal, and this must be due to the fact that something is in the way of collateral circulation that can take up the work of the obstructed vessel which is out of function.

As to the third point, there are certain clinical symptoms which at times permit of the recognition of the disease. I have tried to group these symptoms. Any classification must be more or less artificial, because there is certainly no hard and fast line that can be drawn between any two of these groups of cases.

The first group that I have put down as caused by obstruction of the coronary vessel is that in which death is seemingly instantaneous. These are the cases that have been described particularly by Krehl, who emphasizes the fact that there is a sudden stoppage of the heart and respiration; there is no agonal struggle, no edema of the lungs, no distortion of the features. Death seems to be extremely sudden, or, we may say, instantaneous.

A second group would be those in which there is obstruction, with heart pain; there comes sudden or early death, within a few minutes or a few hours. If the physician reaches the house in time, he sees that the patient is clearly in the death agony.

The third is the group in which the symptoms are severe, but death is deferred for hours, for days, for months, and possibly recovery occurs.

The fourth is a group that is purely hypothetic. The patient's symptoms are slight; possibly there is a slight pain. It may be passed off as a neuralgia or pleurodynia. In many hearts there are scattered patches of fibrosis, many of which are surely due to obstruction of the twigs of the sclerosed coronary. If a large branch may cause sudden death with pain, why not a small twig produce slighter symptoms without death?

It is of the third group particularly that I am speaking tonight. These patients as a rule are from 30 to 50 or 60 years of age; some have signs of definite cardiovascular disease; some have not. Some have suffered previously from typical angina pectoris on walking, etc. In all the cases in which I have dared to venture this diagnosis, pain has been a striking feature. The patients who have previously experienced angina describe the pain in this attack as the worst they have ever had. The pain may be substernal or precordial, may be referred to the epigastric region, and may or may not radiate to the arms. It is rather diagnostic of this type that the pain has lasted longer than in typical angina. It may last a half hour, or 3, 4 or 5 hours, and in one or two cases I have seen it amount to a typical status anginosus in which one severe attack succeeded another. Huchard said that in some of the cases that he describes there was no pain. Not infrequently the pain has stopped after a few hours, even though the patient lived for a long time. Often there is nausea with vomiting; the patient is frequently in a condition of collapse. A striking fact is that the mind remains clear.

The pulse is generally small in volume, though sometimes the volume is fair; it is sometimes almost imperceptible, frequently rapid, more rarely slow, frequently running, sometimes irregular. The heart tones are startlingly feeble. The blood pressure is low, and it is rather characteristic, at least of the cases going on from bad to worse, to have the blood pressure hour after hour get lower and lower. Dr. LeCount spoke of a fibrinous patch over the area of softening of the heart. Pericardial friction is not infrequently heard over the infarct in the myocardium. Twice I have heard this. If the patient lives a few days or weeks he generally shows signs of myocardial weakness. This may be extreme, as in two cases in which there resulted edema of the legs,

ascites, albuminuria, etc. In other cases the symptoms are those of chronic fibrous myocarditis—dyspnea on exertion, anginal attacks, cyanosis, cough, etc.

A rather striking fact is also the acutely developing emphysema. The first case I ever saw puzzled me. There was a marvelous hyperresonant note over the chest, obscuring the cardiac dulness, and only when I looked up the subject did I find that von Basch had already described it. Frequently there are râles due to edema of the lungs. Some of the patients I have seen have impressed me not only on account of the clear mental condition in spite of the startlingly feeble circulation, but by the way in which they preserved their muscular strength. Yet in one or two I have seen an asthenia comparable in its degree to that of pernicious anemia or Addison's disease. Many attacks resemble closely a surgical subdiaphragmatic accident such as pancreatitis or perforated gastric ulcer.

I have seen one case in which I believe there was coronary obstruction with a most remarkable after-effect. A man described to me having had frequent attacks of angina after walking, for several months. One day he had a frightful attack of the character I am describing and which I thought was due to coronary obstruction. Following that he had no attack of the ordinary paroxysmal variety. I do not know how to explain that unless it is like this: I can conceive that this man had a roughened coronary vessel partially obstructed, which after the manner of intermittent claudication produced on exertion the painful seizure. Then a thrombus formed at some narrow point, and this put a certain portion of his myocardium out of function with resulting fibrosis, to which new condition the heart became accustomed and which did away with the varying and relative ischemia of the myocardium that was present when the obstruction was partial but sufficient to interfere with the blood supply adequate to meet the demands produced by exertion.

I believe it is possible in many of these cases to make a fair approximation to a diagnosis, and I have been led to that belief because in 3 cases in which the clinical symptoms were carefully studied, necropsy showed coronary obstruction. These were cases in which there had never been a previous attack of angina, in which there was no marked sclerosis of the beginning of the aorta; they were in 3 persons who had never had syphilis, and yet the coronary artery in each one was distinctly sclerosed.

At my suggestion Dr. Fred M. Smith in the Presbyterian Hospital and Rush Medical College studied experimentally the coronary arteries in dogs. He first injected the arteries of the heart. Some anastomoses could be seen with the naked eye. At times, as he injected, he could inject the right coronary from the left, or vice versa. The objection Dr. LeCount raised to many of these studies is valid. Dr. Smith tried not to use too much force, registering the pressure with a mercurial manometer. The second point he tried to establish was the mortality from ligation. His results in animals are more favorable than Dr. Porter's and compare favorably with those of Dr. Miller. Thus 1 dog out of 11 in which he ligated the ramus descendens of the left side died; 10 lived. In the circumflex the mortality is always higher. These experiments concern acute obstructions. I believe, with Dr. LeCount, that there is a great field for experimental work in producing slowly forming obstructions.

The third point was the determination of the area of the heart muscle that became softened and later fibrous as the result of the obstruction of each artery or its branches. It was possible to produce with reasonable certainty lesions in a fairly definite area by ligation of various arteries. In general the endocardial and subendocardial changes were more extensive than those in the subepicardial tissue.

Lastly he studied the electrocardiographic changes produced by these obstructions. He took the dog's electrocardiogram before operating. Tracings were made soon after the operation to get the immediate change; then at varying intervals, from a few minutes up to hours, days, weeks and months, and the irregularities were noted. Careful study was made of the hearts of dogs dying or killed. The thought in this work has been that if it can be proved that with a certain artery obstructed there is a definite lesion in the heart muscle or in the conducting system, and if with that lesion there is a definite electrocardiogram, may it not be that when we encounter that abnormal electrocardiogram in the human being and have the symptoms suggestive of coronary thrombosis we may be able to state with a reasonable degree of certainty that the patient has had obstruction in a particular portion of the coronary system?

It takes a long time to reach any results in the human being. Patients with this condition do not present themselves very often; a large proportion with coronary obstruction die a sudden death, or are too ill to come to the office or to a hospital where they can have the electrocardiographic tracings taken. And yet we have been able to take several tracings in patients in whom we believe these coronary thromboses had occurred. And in one of the cases the patient died, having lived 5 months after the obstruction. The electrocardiograms turned out to be right. The necropsy revealed the lesion.

[Dr. Herrick showed lantern slides illustrating the experimental work of Dr. Smith, including tracings from dogs, which were compared with some from human beings believed to be suffering from coronary obstruction, the diagnosis in one case having been confirmed by necropsy.]

DR. ROBERT H. BABCOCK: Allbutt limits the term "angina pectoris" to Heberden's classical syndrome, and rejects the terms "true" and "false" angina, believing there is but one angina; that the other pains which are sometimes considered angina should be called spurious and mock anginas; that these pains are frequently associated with certain vasomotor phenomena which Landois and Nothnagel term "vasomotoria" and "reflectoria," terms which Allbutt rejects because calculated to obscure the subject in hand. He prefers the classification for these cases of Sir William Gowers, that they are vascular disorders. Allbutt's view of the nature of angina is this: that the angina of Heberden is a pain located in the ascending artery, or in the suprasigmoid portion of the ascending aorta, and that this pain is due to tension or stretching of the fibrous coat, the adventitia. Since, he says, pacinian corpuscles have been demonstrated in the fibrous coat of the artery, in this respect the pain is like the pain of intestinal colic, or any pain caused by stretching of the fibrous investment of some abdominal structure or dragging or pulling on the omentum. He believes the cause of this pain is an aortitis which may be a chronic, a subacute or an acute aortitis, or may be a chronic aortitis with acute exacerbations. He regards as the proximal causes of this aortitis the usual factors which are more or less definitely recognized in the causation of senile atheroma of the aorta or of the arteries, but especially 3 influences—syphilis, influenza and rheumatism. In substantiation of this view he cites almost innumerable cases illustrating the causes of angina in comparatively young people, in whom syphilis would cause aortitis. He also cites cases in young people, even in children, in the course of acute rheumatism, and one or two cases in which necropsy revealed that there was an acute aortitis in these children in addition to rheumatic infection of the heart muscle or valves.

Now he says he cannot attempt to discuss all of the 80 hypotheses of angina that Huchard had collected, but discusses the principal one, namely, coronary disease and cramp of the coronaries, spasm of the heart muscle, dis-

tention of the heart muscle, etc. In discussing coronary disease he calls attention to the fact that one might say the majority of old people show more or less coronary sclerosis after death, and yet the majority of such people never suffer from angina. On the other hand, he cites many cases of people who die, having suffered from typical angina, in whom the coronaries were not diseased at all—disease could not be found. He criticizes clinicians and pathologists alike for not investigating carefully the condition of the adventitia of the artery, saying that they usually content themselves with the statement that the aorta shows more or less sclerosis, and in syphilis they study the intima and media, but rarely, if ever, the outer coat of the artery. He doubts that the heart muscle itself is capable of pain, because the ganglions and nerves of the heart, he believes, are motor rather than sensory; nevertheless, when disease of the heart does produce pain, he thinks the pain is caused by tension of the fibrous investment of the structures of the heart. He admits that pain occurs in coronary thrombosis or coronary occlusion, believing that when pain, as Dr. Herrick has said, occurs as the result of coronary occlusion it is the result of sudden blockage; and he quotes Kaufmann that it is only sudden occlusion of a main coronary artery which produces pain. Nevertheless, he believes that the pain of sudden blockage of the coronary artery from embolism, for instance, can be distinguished, and is to be distinguished, from typical Heberden's angina, and he gives exactly the symptoms which Dr. Herrick has mentioned, not only that the pain is frequently pericardial or epigastric, but that there are certain other associated symptoms which do not properly belong to Heberden's angina, namely, dyspnea, disorders of the pulse, as Dr Herrick has said, failing circulation, failing heart and lowering blood pressure; whereas in typical angina the pulse is rarely altered to any appreciable extent. It may be slowed a little, or increased a few beats. The blood pressure, however, is variable. In some cases it may fall; in others it remains unaltered, while in others it rises, and he cites various observations from such observers as Mackenzie that there is nothing constant in the blood pressure during angina, for it certainly does not always fall, nor are there always symptoms of collapse, edema of the lungs, vomiting, etc., as in coronary embolism. He would regard such symptoms, if they occurred, as epiphenomena and due to associated lesion. He believes the sudden death in Heberden's angina is due to inhibition, and that it is a manifestation of the impression made on the vagus by the pain. If an attack of gallstone colic can produce pain by inhibition, as he witnessed in one young woman whose heart showed absolutely no disease, then how much more easily may a diseased heart be stopped through the influence of pain on the vagus. In further corroboration of his theory he cites the pain of pericarditis, but gives cases showing that when angina has been present in cases of pericarditis that have come to necropsy sooner or later, the changes of pericarditis were found at the root of the aorta where the pericardium is reflected over the roots of the aorta. And this reminds me of the statement of Dr. LeCount that in case, as he says, the circulation at the roots of the aorta is provided by the anastomoses with other vessels, may not that very change in the coronary vessels in this situation lead to changes in the outer or fibrous coat of the aorta, which changes themselves may be responsible for the angina? I am not here to defend Allbutt's view, although I will say it appears to me as a hypothesis likely to explain the diversity of findings which are recorded, and the reason why so many investigators have such very different views concerning the nature and cause of the pain.

Allbutt rejects the theory of the angina's being due to distention of the heart muscle, citing the statements of the late John H. Musser and other authors to the effect that they had recognized cases of typical angina in which the angina totally disappeared after dilatation set in and mitral insufficiency became established, and reappeared with the return of compensatory hypertrophy. I think Allbutt would assume that in such cases the dilatation lessens somewhat the strain brought on the suprasigmoid portion of the aorta and therefore does away with such tension and stretching of the sensitive coat of this portion of the vessel as to bring about angina. He believes the theory of spasm of the heart muscle is not tenable, since, as he asks, What is systole but transient spasm of the heart muscle? Spasm of the coronaries and intermittent claudication he looks on as makeshift views to explain the great variety in the morbid anatomic changes found in the hearts to which I have alluded. In some hearts suffering with angina the coronaries were not diseased, and in others they were greatly diseased. On the whole, Allbutt, it seems to me, has presented a very strong case, and whether it answers to all cases or not, it certainly does seem to me that his views explain the overwhelming majority of cases, both in their causation and in their symptomatology, and we may say also in those measures which relieve angina.

ANGINA PECTORIS: REPORT OF A POSTMORTEM EXAMINATION

E. R. LeCount

This examination concerns the case of angina pectoris described by Dr. E. F. Ingals.[1]

Anatomic Diagnosis. — Marked senile arteriosclerosis (cerebral, coronary, aorta, pulmonary, celiac, renal and right axillary arteries); occluding thrombosis coronary arteries; disseminated fibrous myocarditis; parietal aneurysm of left ventricle; thrombosis of left renal artery; hypertrophy of heart; terminal dilatation of mitral and tricuspid rings (decompensation); fresh subendocardial hemorrhages; anasarca and hydrops with edema of lungs and leptomeninges; disseminated focal arteriosclerotic atrophy of cerebral cortex; diffuse dilatation of basilar artery; saccular aneurysm of right iliac artery; passive hyperemia of spleen, stomach and esophagus; cyanotic atrophy of liver; chronic hypertrophic gastritis; hypertrophy of prostate with valvelike formation of middle lobe; proximally elongated urethra; hypertrophy and dilatation of urinary bladder; bilateral hydro-ureter and hydronephrosis; multiple spurs (pseudo-valves) of ureters; almost total pressure-atrophy of left kidney; gouty phalangeal joints (tophi); senile porosis of ribs and sternum; chronic obliterative appendicitis; fibrous obliteration of right pleural cavity; hyperplasia of tracheobronchial lymph glands; moderate coal-dust pigmentation of lungs, tracheobronchial and biliary lymph glands; slight fat infiltration of pancreas; patent foramen ovale.

Extracts from the record.—The body of a white man about 5 feet 7 inches long, and 70 years old. Dependent parts of trunk, extremities edematous; no rigor mortis except in jaw; body still warm and posterior lividity slight; a number of joints of hands, especially distal phalangeal, enlarged; trunk heavy, arms markedly emaciated.

The skeletal muscles are pale; peritoneum smooth; bladder distended with urine with vertex 15 cm. above upper margin of symphysis pubis; 200 or 300 c c clear fluid in abdomen; appendix a slender fibrous cord for its distal two-thirds and bound to mesentery; diaphragm on each side a little low.

Left lung free; pleural cavity contains about 75 c c of clear fluid, right pleural cavity replaced by loose fibrous adhesions; right lung firmly adherent to pericardium; fully twice normal amount of clear fluid in pericardial sac; no changes in lungs except edema.

[1] Proc. Inst. of Med. of Chicago, 1918, 2, p. 50.

Perirenal fat abundant. The right renal pelvis is about twice normal size and the medullary pyramids are small from pressure atrophy; in proximal half of right ureter three spurlike valves with intervening dilatations; capsule strips easily; surface a little granular; in the upper pole a retention cyst 1.5 cm. dia.; cortex lessened, one-third striations closely set. The change in the left kidney is similar but much more marked, a mere shell of parenchyma being left, 5 mm. thick and in many places less, and there is a huge dilatation of renal pelvis and calyces, with spur valves in left ureter; a light brown thrombus in left renal artery. Adrenals normal.

The abdominal aorta cuts with increased resistance. There is a small sacculated aneurysm about 1 cm. in diameter, of the outside of the right iliac artery filled with a clot partly lime; about one-third or one-fourth of lining of abdominal artery is atheromatous with ulcers with some lime; lime absent from yellow thickenings of most of lining of thoracic aorta. Beginning of aorta appears quite normal.

There are small patches of yellow thickening of lining of pulmonary artery and branches out to third division.

The heart with 1.5 cm. of the pulmonary artery and 1 of the aorta weighs 470 gm.; the aorta with 4-5 cm. of the iliac arterior 90 gm. The mitral ring admits 5 fingers easily, the tricuspid 6. There is a little loose clotted blood in the left ventricle. The tricuspid ring without stretching is 15.5 cm. in circumference; the front wall of the right ventricle 1 cm. thick, in the pulmonary conus 1.3 cm. There is a small oblique opening between the auricles at the front margin of the fossa ovalis, which is large, circular and 3 cm. in diameter. The fat of the front of the right ventricle at the base is 1 cm. thick. The proximal two-thirds of the posterior coronary artery is rigid and no part of the lining of this portion of the artery is free from change; raised yellow patches alternate with dark sunken areas. At the mouth the channel abruptly narrows and this constricted place 2-2.5 mm. in diameter, occupies the proximal 6 mm. Beyond the narrowing, the channel quickly is enlarged to a circumference of 14 mm.; 8.5 cm. distal to the mouth the channel is closed for 6 mm. by a firm clot, obviously of some standing, and beyond this where the descending branch is given off, the channel is again open. The beginning of the descending branch of left coronary artery is rigid, the channel about half the normal size and 2 mm. distal, the lumen is obliterated or reduced to a minuteness barely visible; these changes end abruptly 4.5 cm. beyond the division of the artery. The circumflex branch of the left coronary artery is but little changed; its circumference 12 mm. at its beginning suggests compensatory circulation. All through the myocardium is fibrous tissue. The outer wall of the left ventricle measures 18 mm. thick at the base, 10 in the middle and at the apex 2 to 3. The middle of the septum between the ventricles is 12 mm. thick. The circumference of the mitral ring is 12.5 cm. Some of the papillary muscles for the back mitral leaflet are mottled with white fibrous tissue and much smaller than normal. The aortic leaflets are without change and the mitral also, except for 2 small yellow patches in the front leaflet more visible in front. The lining of the heart is otherwise normal. In cutting the myocardium, a small hemorrhage 2 mm. in diameter is found in the front wall of the left ventricle near the apex and here, more in the interventricular septum than the outer wall, is a great deal of fibrous tissue. The auricles have thin walls translucent between the muscular ridges, and the appendages are empty; the large coronary sinus has a smooth lining.

[illegible]

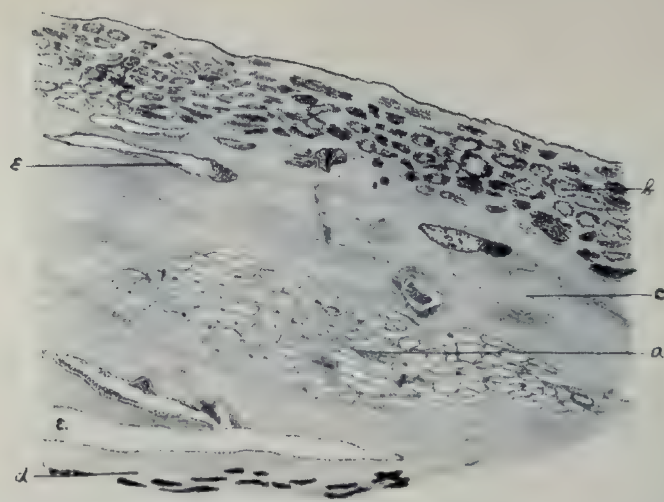

Fig. 1.—A spindle-shaped patch (*a*) 1.5 mm. long filled with remains of muscle fibers all but disappeared from hydropsical degeneration — edema and surrounded by scar tissue; (*b*), subendothelial muscle fibers, the seat of less marked edema; (*c*), scar tissue; (*d*), scar tissue with scattered muscle fibers but little altered; (*e*), veins. (Phosphotungstic acid hematoxylin).

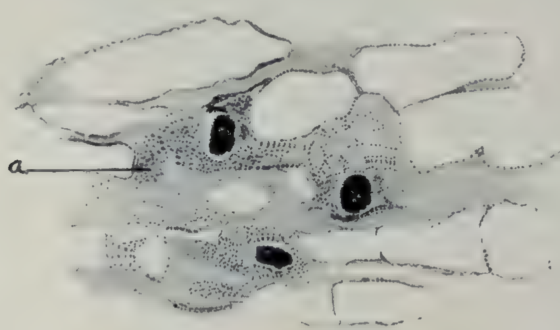

Fig. 2.—An immersion-lens detail of the patch shown in Fig. 1. With phosphotungstic acid hematoxylin the cross-markings of the minute fibrillae (sarcous elements) of the muscle fibers stain very distinctly. They remain longest about the margins of the spaces formerly occupied by the muscle fibers. (*a*), a mass of the brown granules of pigment so common at the ends of the nuclei of muscle fibers.

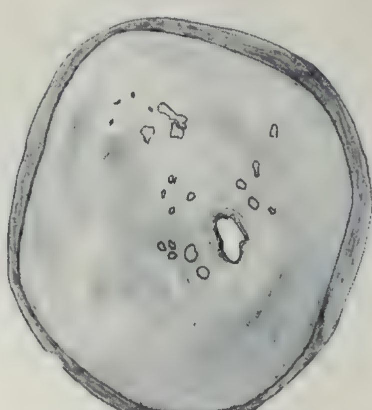

Fig. 3.—To illustrate the minute channel and recanalizing vessels in the obstruction of the right coronary artery 8.5 cm. distal to its mouth where the descending branch arose. The outer darker ring represents the media; no attempt is made to represent the adventitia. The large oblong channel near the center is the only part of the original channel of the vessel remaining in the sections examined.

Microscopic examination.—In section (7 by 8 mm.) from the front of the left ventricle near the apex, fully one-half is old scar tissue; in those (11 by 12 mm.) from the middle of the interventricular septum there is a strip of fibrous tissue along one edge for 11 mm. and 1-1.5 mm. wide, with smaller patches deeper in the sections. Single muscle fibers cut off and within the scar tissue as well as others near its edge are edematous; in phosphotungstic acid hematoxylin preparations the ultimate fibrillae — anisotropic elements — in these swollen fibers are very distinct in a few cells, but only at the margin; for the most part they are absent (Fig. 2). In sections (7 by 16 mm.) from the middle of the outer wall of the left ventricle there is no change but a little edema and those (7 by 13 mm.) from the muscle for the front mitral leaflet are similar. In section (15 by 5.5 mm.) from the outer wall of the left ventricle near the base there are a number of small patches of scar tissue with one much larger, 1.5 mm. long and one-fourth to one-fifth as wide; those (10 by 3 mm.) from the papillary muscle for the back mitral leaflet — grossly "mottled with fibrous tissue"— are from two-thirds to three-fourths fibrous tissue deep pink with phosphotungstic acid hematoxylin. Many of the muscle fibers here are in all degrees of edema. In the center is a patch of fibrous or scar tissue and in its middle a place spindle-shaped in single sections 1.5 mm. long and 0.5 mm. wide (Fig. 1) filled with the spaces as a mesh work from which the muscle fibers have disappeared by real "hydropsical degeneration"; the scar tissue is as ancient as in any other places. In these various sections of heart muscle there is no necrosis or leukocytic infiltration or other evidence of acute change in or about the scattered patches of fibrous tissue.

Many sections from different parts of the first 20 cm. or so of the aorta show no special changes. Nothing but the retrogressive changes and patches of thick intima common to senile arteriosclerosis are seen in sections of the aorta in the ascending part, and in many places beyond in the thoracic and abdominal portions. These sections are in general about 2.5 cm. of circumferential segments, about one-third to one-half the circumference. They contain no cellular exudate in the adventitia in any place of most change; the vasa vasorum are normal. The new collagen and scattered muscle fibers and relatively little elastic tissue of the thick intima of the right axillary artery is more of a true endarteritis than any of the intimal aorta thickenings. The obstruction in the posterior coronary artery in its circumflex branch resembles an organized thrombus of long standing with some recanalization (Fig. 3), for in the new tissue almost occluding the lumen there are a number of thin-walled new blood vessels, adventitious channels which in the sections examined have a combined area equal to if not greater than the remainder of the original channel. The wall here is 3 mm. in diameter and the remains of the true channel one-third to one-sixth of a mm. in diameter.* In the left renal the obstruction is also thrombotic, some of it recent, the lumen reduced to one-third its normal size, the obstruction all within the inner elastic layer between media and intima, the thrombus partly organized with new blood vessels in it, small masses of blood pigment and old fibrin. In the sections examined of the pulmonary artery, changes similar to those in the aorta are present; in some of these are greatly dilated lymph channels in the adventitia. In the little arteries about ½-1 mm. in diameter in and about the capsules and fibrous tissue around lymph glands, the adrenals, the epididymides, in the submucosa of the stomach and bowel and similar places in other organs,

* Such measurements as these are readily made from a table of the diameters of the fields of the various objectives with the different eye pieces estimated carefully with stage and eye-piece micrometers.

there is no change. Those in the kidney sections, on the other hand, have the thickened inner coats commonly present with so much of loss of renal parenchyma.

In sections of the kidneys, spleen, liver, genital organs, stomach, large and small bowel, pancreas, adrenals, lungs and lymph glands from various sites, there is but little not already noted in the gross examination; edema, hyperemia and terminal or agonal deposits of fibrin in blood or lymph vessels are present.

The distinctly focal character of the almost total occlusions of the coronary arteries, as well as the evidence of long standing of these and of the scars in the heart muscle, indicate that during the long illness, there was in all likelihood some compensatory anastomosis established between various branches of the coronary arteries. The suggestion by Allbutt that the symptoms of angina pectoris are due to alterations in the aorta or elsewhere outside the heart, finds but little if any support from the conditions found by this postmortem examination; in fact, nothing was found in the aorta to associate with the radiating pains. Moreover the lesions present all point to the maintenance of life for an unusually long period by a heart with a markedly damaged blood supply.

Robert Tracy Gillmore, 1867-1918

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ROBERT TRACY GILLMORE
1867-1918

It is our mournful privilege to present a brief memorial of our associate and friend Dr. Robert Tracy Gillmore, who died in the service of his country Jan. 20, 1918. It was the termination of a life that had attained the very flower of professional usefulness and mental growth.

Born Sept. 9, 1867, Robert passed his youth in studious preparation for the medical career he had resolved to undertake. He began his actual course in medicine at the University of Michigan where he met and married, in 1890, his wife, Dr. Emma Hastings Gillmore who now survives him.

Soon after their marriage, the young pair came to Chicago where Dr. Robert entered the class of 1892, then the senior class of the Northwestern University Medical School.

After graduation he went to Denver, Colo., and for 4 years was engaged in general practice and gynecology in association with Dr. Fleming.

The tie of attachment to his Alma Mater was too strong, however, to permit him to settle permanently in the west, and in 1896 he returned to Chicago and began the practice of gynecology as a specialty. In this field he soon became widely known for his conscientious acceptance of his responsibilities and for his masterly technic.

Meanwhile his medical connections became stronger and more numerous. He was a Fellow of American Medical Association and a member of the Chicago Medical Society which he served as secretary for 2 years. He was a Fellow of the American College of Surgeons and of the Chicago Gynecological Society which he also served as secretary and president. In addition, he belonged to the Chicago Pathological Society and to the Chicago Institute of Medicine, and when he entered the Army he was attending gynecologist to Wesley Memorial Hospital and clinical professor of gynecology at the Northwestern University Medical School.

In 1917, Dr. Gillmore accepted service as a captain in the Medical Reserve Corps, and was ordered to Fort Oglethorpe, where an accidental infection of his arm brought his life to a close after an illness of only 4 days.

His death was both a professional and a personal loss. As a teacher he was unusually felicitous, his success apparently being due to a certain directness of speech, the extreme practicality of his discourse and the abundance of his information rather than to eloquence and impressiveness of manner.

As a practitioner he was widely popular on account of his consecration of purpose and his unwearying self-sacrifice to the needs of his patients.

His friends, however, will miss him most keenly. Dr Gillmore was a sincere friend and an ardent advocate of any cause that enlisted his support and, being a man of strong feelings and high ideals, his advocacy was sometimes more direct rather than diplomatic, yet, while sometimes abrupt in manner and impulsive in action, no one ever questioned the sincerety of his motives or his personal integrity.

His friendships were not numerous, but he possessed a quality of eternal boyishness that made them very intimate and, when once formed, the bond was an unbreakable link of gold. Loyalty to these friends and to the guiding principles of his life was the most marked characteristic of Dr. Gillmore, and fortunate was the friend and fortunate was the cause whose defense he undertook. His faith was unflinching, his ardor untiring and his courage inexhaustible. He partook of the fruit of life in that "the world is better for his having lived."

CHARLES B. REED,
A. I. KENDALL,
THOMAS J. WATKINS.

HANDLING OF THE VENEREAL PROBLEM IN UNITED STATES ARMY

William Allen Pusey
Chairman, Committee on Venereal Diseases for the Surgeon-General of the Army
April 26, 1918

If we could handle venereal diseases as we can other infectious diseases they would offer a relatively simple sanitary problem. We know all of the facts necessary for their sanitary control. We know their causes, their incubation periods, and their modes of transmission; and these facts so far as they are physical facts offer no practical obstacles to sanitary control. But for all that some sanitarians may say, the venereal diseases cannot be handled simply as a sanitary problem. No effective policy is practicable which would isolate them like measles or scarlet fever; or quarantine them like smallpox; or, even in the present state of sentiment, get them successfully reported. They involve factors peculiar to themselves—social, personal and moral factors that reach into the most insistent and secret impulses of life. These facts make the problem of their control extremely difficult; make it a social as well as a sanitary problem and, without question, the most complex and difficult of social problems.

The Army program has taken full cognizance of both phases of this problem. It can readily be seen that they require very different treatment, and that in coordinating the forces necessary to attack them in a practical campaign, there may be need for tact, judgment, tolerance and sympathetic cooperation. In this attempt the dangers are many, of cross purposes, of exaggeration of the importance of one part of the program over the other, of irreconcilable conflicts between radicals on the two sides, especially of having the moral propaganda run away with the medical. We all know to what extremes the sexual moralist can go. How unpractical, how intolerant, how extravagant, even how unreasoning, if not scientifically dishonest, he can be. On the other hand, the medical man can make no boasts of the cool, dispassionate, scientific intelligence that he has brought to bear on the problem. He is usually an infant in the knowledge of the epidemiologic facts of the venereal diseases and of the work that has been done on them as a sanitary problem. If he does not content himself with a mild mistrust of social and moral propagandas for influencing their prevalence, he is

apt to have opinions about what he fondly regards as the practical aspects of the sexual problem, which are not the less vigorous because he has given very little serious study to the subject.

It may be said in passing, I think, that there has happily been an enormous improvement in the intelligence of the medical profession, both civil and military, on the subject in so short a time as the last year.

A very practical proposition has been to avoid the danger of being carried away by extremes in policy in either direction. Up to the present time, however, this danger has not actually obtruded itself.

METHODS OF PREVENTION

All of the methods of attack on the venereal diseases may be grouped into four classes: (*a*) Social measures to diminish sexual temptation; (*b*) education in regard to venereal diseases; (*c*) prophylactic measures against venereal diseases, and (*d*) medical care.

The United States Army at present is carrying out a thoroughgoing attack that embraces all of these various forms of activity. This effort is, I believe, the most systematic, thorough and rational that has ever been made to control this pest. It is a campaign which, aside from its practical results, is of great academic interest to any one who is interested in public hygiene.

The first two groups of measures for controlling venereal diseases are strictly social; and it is in respect to these activities that the most original part of the policy of the American Army consists.

The attempt has been made to utilize all of the social weapons that are practical. And it is an interesting fact that the medical deparment of the Army has been able to get the whole-hearted support of its entire program by all of the organized forces of that new department of sociology that we know as social hygiene. They are unreservedly behind the whole program and are the efficient agents in carrying out the social part of it. When you remember that the medical program has, as perhaps its most important feature, medical prophylaxis of venereal disease, this fact is indicative of the great change that has taken place in the attitude of society, and of the intelligence and wisdom that are now engaged in the extremely difficult work of social hygiene.

SOCIAL MEASURES

Social measures to diminish sexual temptation divide themselves in two sorts of activities: (1) the repression of prostitution and of the liquor traffic, and (2) the provision of proper social surroundings and of opportunities for recreation and diversion.

However unjust it may seem to some, the repression of prostitution and of the liquor traffic are logically classed together. In the spread of venereal diseases they go together. The liquor traffic in numerous ways is the fosterer of prostitution. And the effect of alcoholic liquor is a factor that cannot be overlooked in the diffusion of venereal diseases, because of the inhibition which it produces in those restraining influences that under ordinary conditions prevent man's giving way to his impulses.

It has been recognized, then, by the Army that keeping liquor away from soldiers is of fundamental importance in the program of attack on the venereal diseases. It is not necessary to go into the measures which the government has enacted to keep alcoholic liquors away from the soldiers. It may be said, however, that these measures are being enforced, and that the amount of alcohol consumed by the present Army of the United States is negligible. There is an occasional boot-legger, and a small amount of liquor gets to the soldier in devious ways; but it is, in the total, inappreciable. For all practical purposes the United States Army at the present time is a body of total abstainers. This fact is undoubtedly a very great factor in keeping down in the Army the incidence of venereal diseases.

The control of the liquor traffic and of prostitution has been one which has called for cooperation between federal and local authorities. Of course, inside cantonments and other government reservations the federal authorities are supreme. In addition to this federal area, a district has been provided by law, consisting of a zone, at present designated by the Secretary of War to be 5 miles, around each of the cantonments. In these zones the federal authorities are in position to control completely the liquor traffic and the various conditions which encourage prostitution. Even, therefore, where cantonments are situated near districts presenting the worst social conditions, the gov-crnment is able to make prostitution difficult, and is very effectively doing it.

Outside the zones, the federal government can still exert great influence as regards these conditions, and, as necessity compels, is doing this. But for the most part, when it comes to the question of controlling prostitution and liquor traffic outside the zones, reliance has been placed in great measure on the local civil authorities. I think it can be said with considerable satisfaction that communities have

almost without exception realized their responsibility in these matters and have responded as well as the most sanguine could have asked in their efforts to improve them. Cities have cleaned up in the last few months that have never cleaned up before; to such an extent is this true, that conditions in regard to prostitution in this country are the best today that they have ever been.

The cause of this is the awakened public conscience; the determination of our people to do the best they can for their soldiers. To attain this, much has been done in directing the public conscience, in discovering the conditions that need correcting, and in showing the public useful avenues of work.

In this ticklish business the Army is not trusting to well meaning amateurs alone. It has its own trained forces in the field, recruited largely from the experienced workers of such organizations as the American Social Hygiene Association. Vice conditions are minutely studied, and are known with a fulness that is surprising. Often, as a result of this, the condition of prostitution in a community has been revolutionized for the better almost in a day. More often the improvement is less magical. But the pressure is everywhere, most about camps, and is resulting in rapid betterment.

The interest of the intelligent public, not merely of the intellectual classes, but of the every-day citizen, in the menace of venereal diseases, has been accumulating in the last few years. The war has stimulated this to a point at which you can get the public to support any policy concerning them that is sane and useful. This makes the present time a unique opportunity for attacking the problem, and sanitarians are showing a disposition to utilize it. Everywhere the work for the control of venereal diseases is stimulated and many new approaches to the problem are being developed.

You can hardly find a district where there is not some manifestation of this activity. New and better ordinances and sanitary regulations in regard to venereal diseases are being enacted, and more intelligence is being applied to their enforcement. Municipal clinics for the treatment of venereal diseases are being established. Established clinics are being reorganized to do better work. Hospitals for venereal diseases are being provided; even, in some places, isolation hospitals for venereal cases are in operation. Evidence of this sort of activity is found everywhere from the Atlantic to the Pacific. There has never been any systematic widespread attack on venereal diseases in the

country before. There is now an almost universal and, for the most part, intelligent attack carried on.

The state councils of defense have generally taken up the work in their various states. Private organizations interested in public welfare are helping the campaign in innumerable communities. The aggregate, therefore, of work which is being contributed by forces not directly controlled by the federal government is not easy to be estimated.

The second group of measures to diminish sexual temptation are embodied in the provision of proper social surroundings and recreations. Applied to the Army, this means the furnishing of healthy social conditions and of opportunities for diversion for the soldiers at periods of leisure in camp, or when they are traveling, or on leaves of absence outside of their camps. In the camps the government has through the Commission on Training Camp Activities pursued a policy which, it seems to me, is of the highest intelligence in regard to the provision of recreations. The situation has been conceived to be much the same as that of a college community, where there are a large number of young men brought together, who have recently been detached from their familiar home surroundings; and it has been handled with college activities as the example to be followed. All of the wholesome forms of play which constitute the familiar recreations of college life have been included, and are encouraged and supported. The effort is to create the same sort of a class spirit among the men; to get them interested in their diversions and to excite in them a pride in their sports as in their work.

In furnishing proper social surroundings and facilities for recreation in the camp, the authorities have availed themselves of the invaluable experience of organizations which have been working so long in these fields of civil life, such as the Y. M. C. A., the Knights of Columbus and the Y. W. C. A. These organizations are not only doing incalculable work for the soldier in the cities; they are doing a greater one in the camps, where they have adapted themselves to military conditions.

Outside the cantonments and the zones, there has been an appeal to the civil population to add their part in this work. I think you are all more or less familiar with the cordial response which the public has given to this appeal. Hardly a community (no community that I know of) has failed to respond to this appeal to aid. What some communities have done amounts to examples of almost illimitable hospitality.

Petersburg, Va., a town of about 30,000 inhabitants, has 7 places of entertainment—clubs, canteens, or recreation centers—which are regularly open for the soldiers at Camp Lee, located near the city. Houston, Texas, which has a population of about 90,000 inhabitants has 10 such places, and Montgomery, Ala., with a population of about 50,000, has 12.

In some of the towns near cantonments every home has been opened to the soldiers and they have been given the hospitality that is offered to the most welcome friends. Every community and every organization is trying to do its part in providing wholesome social diversions for the soldiers. Among organizations, the work of the Y. M. C. A., Knights of Columbus, Y. W. C. A., and the Masons represent the largest efforts, but every organization that has any sense of social responsibility is doing something.

In many cases the efforts have taken very interesting practical form. The establishment of lunch counters and cafeterias which are manned by voluntary help and located at such centers as railway stations, for furnishing appetizing food at little or no cost for soldiers, is one illustration. Information bureaus are another.

The most useful thing of this sort, I believe, is the establishment of the enlisted men's clubs—clubs which are the men's clubs, where they can go freely and feel that they are at home. I have seen some of these clubs which were extensive enough and well enough equipped to be private social clubs of considerable pretensions.

I recall one such club in which the first floor is a reading room about 50 by 150 feet in size, comfortably furnished throughout—rugs on the floor, bookcases around with a good supply of books and magazines, most of the papers from the homes of the troops who frequent it, plenty of good chairs and lounging places, phonograph, piano and other musical instruments. And this lounging room was not the old style parlor not used by any one; at the time I visited it, it was filled with young fellows evidently at ease and thoroughly enjoying themselves. Enlisted men have not reached the age at which they are nervous and finicky. They are reading, playing checkers, writing letters—without irritation, at peace with the world, while the room was joyful with more or less musical sounds from phonograph and piano. It was as orderly a crowd as you would see in a university club (and just as intelligent looking); and the manager told me that the question of order had been no question to him at all, the men taking care of that

themselves. The second floor was a pool room with 11 pool tables, every one of which, by the way, had been resurrected from the storeroom of some person who at some time had thought he would like to have a billiard table in his home and finally had discarded it. The third floor was fitted up for entertainments. There picture shows, dances, popular lectures and various sorts of entertainments are given, furnished by voluntary talent.

TABLE 1

CITIES THAT MAINTAIN ONE OR MORE CLUBS FOR SOLDIERS

Alexandria, La. (2)	Highland Park, Ill.	Norfolk, Va.
Atlanta, Ga. (1)	Jackson, Mich.	Patchogue, N. Y.
Ayer, Mass.	Kalamazoo, Mich.	Palo Alto, Calif.
Beaufort, S. C.	Kansas City, Mo.	Petersburg, Va. (4)
Boston	Lake Forest, Ill.	Philadelphia (3)
Charleston, S. C.	Lawton, Okla.	San Antonio, Texas (1).
Charlotte, N. C.	Leavenworth, Kan.	San Diego, Calif. (3)
Chattanooga, Tenn.	Little Rock, Ark.	San Francisco (2)
Chillicothe, Ohio.	Louisville, Ky. (2)	Seattle (1)
Columbia, S. C.	Macon, Ga.	Spartanburg, S. C. (1)
Deming, N. M.	Manhattan, Kan.	Southport, N. C. (1)
Des Moines, Iowa.	Montgomery, Ala.	St. Louis (1)
El Paso, Texas.	Mt. Pleasant, S. C.	Tacoma, Wash. (1)
Fort Worth, Texas.	Newport, R. I.	Trenton, N. J. (1)
Hempstead, N. Y.	New York City.	Waco, Texas (4)
Houston, Texas.	Nogales, Ariz.	Waukegan, Ill. (2)

When my list was made up in January, 1918, there were in the United States 67 of these clubs, usually under the name of Enlisted Men's Clubs, or Soldiers' Clubs, located in the cities mentioned in Table 1.

This list is, I know, incomplete, and in it I have not included canteens, rest rooms, Y. M. C. A. rooms, or innumerable places of entertainment or hospitality for soldiers, which cannot be called clubs; it is a list of clubs for soldiers.

These enlisted men's clubs are one of the very useful institutions in communities where soldiers habitually come on leave or where they collect in their travel. They supplement the work of the welfare organizations and the fraternal orders and reach those men who are not reached by such organizations as the Y. M. C. A., which to some men, in spite of every effort to avoid it, still have the atmosphere of propaganda.

It does one's heart good to see how much effort in the direction of promoting the comfort and welfare of the soldier has been accomplished. It is a credit to the spirit of the American people. There is still a great deal to be done, but what is lacking, I think, is due for the most part, not to the reluctance of the people to furnish the facilities, but rather to their uncertainty as to what is wanted of them and

what is best. In the way of furnishing information on these things there is room for intelligent direction. The furnishing of this is rather difficult. It requires that there shall be found representative people in each community in whom the community has faith, who can first be interested in the need for the soldier and then can get the ears of their community.

In all these matters that relate to the soldier, the response of the public has been, as I have already said, remarkable. The situation is such now that you can get the public behind any proposition no matter how difficult it is for them, as soon as you convince them that it is for the good of the young people of the country, for the welfare of the soldiers, and that it is practicable.

EDUCATION

The same civil agencies that have been working against prostitution have been active in the campaign of education of the public in sexual matters and in the dangers of venereal diseases. Education as to the dangers of venereal diseases has been a part of the general campaign. While the work of education has not been as extensive among the civil population as it has been among the soldiers, it has been by the same methods; the aggregate amount of it is very large and is undoubtedly doing a very practical amount of good. Nor has this campaign of education in the danger of venereal diseases been confined to the boys. It has been extended to the girls; and such organizations as the Young Woman's Patriotic League are reaching out to the girls; telling them the danger of venereal diseases and fostering in them a sense of their responsibilities in these matters. The General Federation of Women's Clubs, the Women's Christian Temperance Union, the Y. W. C. A.—such women's organizations as these are giving their powerful support to this work.

When it comes to the soldiers, the work of education is systematic and so thorough that it reaches every man. All of the agencies that have been mentioned already are lending their cooperation in this work. The work is guided and largely done by the War Department Commission on Training Camp Activities and the Social Hygiene Section of the Surgeon-General's Office. Instruction is given by lectures, by pamphlets, and by exhibits and moving pictures. But reliance is not placed solely on measures of general instruction.

Lectures and exhibits and pamphlets for the soldiers in general serve a useful purpose, but they do not reach the soldier that is most in need of them. To reach the soldier in the way that is unfailing and that makes a real impression on him is through his company commanders—the men from whom he takes his orders, and to whom he naturally looks for guidance. Through this channel pamphlets are distributed to him that give safe and unsensational information. But much more telling than this, company officers, both line and medical, give lectures to their men on sexual matters and the danger of venereal diseases. Every soldier is instructed on this subject. This is not a matter left to the volition of the officer; it is a matter concerning which he is under orders and the performance of this duty is seen to by checking up as in other important matters.

It is a difficult thing to get a good popular lecture to young men on sexual matters. In one quarter we get the maudlin; in another the extravagant, sensational and untruthful; in another the unreasonable and impractical; and even when the lecturer is sane, and honest, and wants to tell the truth, it is hard to get actual knowledge of the subject, and harder still to put such a lecture into form. To overcome, as far as possible, these difficulties, company officers are provided with full lectures on these subjects which they can use as such or as a basis for lectures of their own.

The lectures on sexual hygiene and venereal diseases given by company officers to their men are not inane, pseudo-moral stuff. They are plain, serious, instructive talks given by practical men. These lectures reach all of the men; the 2 million men now under arms for the United States have been instructed more systematically and probably more intelligently than any other large body of men have ever been instructed in sexual and venereal subjects. It is not making saints of them; but it is doing a great deal in saving them from venereal diseases.

SEGREGATION OF PROSTITUTES

It will doubtless be noticed that in this program for the repression of prostitution nothing has been said about segregation, and that no part of it includes either the examination or certification of prostitutes. In the program everything possible is tried to discourage prostitution. It is a part of the policy to stimulate activity in providing adequate care of venereal diseases among the civil population, to the end, for one reason, that the numbers of venereal disease "carriers" shall be

reduced as much as possible. There has been a very noticeable access of energy in the public care of venereal diseases as a result of the whole program that we have been considering. But the segregation of prostitutes and the regulation of prostitution in the Continental sense, that is, the examination of prostitutes, their certification and their toleration in definite districts, have not been included in this program, because they have not been regarded as advantageous.

You will remember I have said we have the social hygiene movement of this country for all practical purposes solidly behind this program—behind the whole program. They accept as necessary medical prophylaxis of venereal disease; they fear that it may result to a certain extent in greater freedom of sexual indulgence; but they also recognize that it must be a part of any efficient sanitary attack on the venereal diseases. And they are willing to accept this. But they will not stand for segregation. This is not on moral grounds alone, but it is because in the opinion of conservative, reasonable students, segregation is not an efficient weapon against venereal diseases. It is open to so many abuses that careful observers of it in Europe object to it as a practical measure. In this, in my opinion, they are undoubtedly right, and for this reason, among others, segregation and regulation are not a part of the Army program.

RESTRICTION OF LEAVE OF ABSENCE

It has been suggested to me in more than one quarter that the way to solve the venereal disease problem among soldiers, is not to allow them leave of absence. It is recommended by the Surgeon-General that long leaves should as far as possible be discouraged. Attention is called to the fact that leaves of absence of more than 24 hours are particularly dangerous in respect to venereal disease, and that it is desirable that leaves of absence should be timed so that, if soldiers are out over night, they will return early the next morning to their quarters. This, of course, is in order that in the event they have been exposed to venereal diseases they will most likely not be too late for prophylactic treatment to be efficient. There are some camps in which leaves of absence over night for the soldiers have been prohibited. Among practical Army men I have found usually a strong objection to curtailing too rigidly the leaves of absence. Personally, on general principles, I am not in favor of locking soldiers up in order to prevent venereal disease. It would be easy to prevent new cases of venereal

disease by treating soldiers as prisoners, but personally I would be as much opposed to such a policy as I would be to a policy that would confine every man between the ages of 20 and 30 to the 4 walls of his father's home from 6 p. m. to 6 a. m. It is unfair and is an insult to all of the men who would not need it; and we are not reduced to the necessity of pursuing an impractical policy of injustice and of offering affront to our whole Army.

In an attempt to coordinate social and medical forces in an attack on venereal diseases there is danger that the social forces may be allowed to overshadow and to cause the neglect of proper medical measures. They are so appealing to the moral and religious ideals of human nature, while the medical side has no such call; and the moral propagandist is apt to be intolerant of practical considerations.

There is always the possible danger of an unreasoning propagandist trying to run away with the situation. The fears of this were well expressed by Colonel Lyster[1] of the Army in an article on venereal diseases and the war. He says:

> Now as to our new Army and the future: Higher rates will probably prevail for some time, but hope is backed by knowledge that we have the means, if we can apply them, of controlling this great producer of nonefficiency in armies.
>
> The greatest enemy to its [the Army's] health is venereal diseases. A continuation of the orders and methods successful in the Army from 1908 to date will make a successful answer to that challenge of disease. But no misleading and impractical fanatics must be permitted to have a hand in this question of national efficiency.

As far as I can sense the situation, this danger has not yet materialized.

The two parts of the program have not proved unworkable together, and the forces behind the social program have not minimized the importance of or interfered with the effective administration of the medical program.

MEDICAL PROGRAM

The second division of the program is the medical.

The first part of this is prophylaxis to prevent infection after exposure. This, in the opinion of venereologists, is the crucial part of any program to reduce the prevalence of venereal diseases; omit it and you have omitted the most important single practical weapon we have for fighting this plague.

[1] Jour. Am. Med. Assn., 1917, 69, p. 1257.

This part of the program is in universal effect in the Army and care is taken to see that it is thoroughly carried out. Venereal prophylaxis is a part of the duty of every regimental infirmary and of every other infirmary that has in its care the health of a unit of soldiers. The regimental infirmaries do most of this work and its conduct in the regimental infirmaries may be taken as an illustration of it in general. Everything for giving prophylactic treatment is always accessible in every regimental infirmary. The medical officers are responsible for it and it is carried out by specially trained noncommissioned officers. As far as possible selected men are chosen for these positions. I have inspected a good many regimental infirmaries and I have been impressed by the superior grade of these noncommissioned officers. Such an officer is constantly on duty and the returning soldier can get prophylactic treatment at any time in the 24 hours that he applies for it. This is a matter of general policy and is checked up by medical inspectors. It is seen to, as far as possible, that the conduct of prophylactic treatment is carried out seriously, without allowing an atmosphere of levity or obscenity to creep in.

The prophylactic methods are uniform and are a matter of regulations. They consist in the well known measures. First, there is scrubbing with soap and water; then washing with mercuric chlorid solution of the dilution of 1:2000; a thorough rubbing with 33% calomel ointment; and an injection of 2% protargol, or some of the other trade products of silver albuminate, which are just as effective.

The necessity for medical prophylaxis is instilled into the soldiers' minds. They are universally told that it is not a sure preventive of infection; that the sooner it is applied the more likely it is to be effective; and that after 8 hours it is likely to be ineffective. The taking of it, if exposed, is a matter of army regulation. If a man contracts venereal disease, he is not punished beyond losing his pay while the disease disables him for duty, provided he had prophylaxis after exposure. But if he contracts a venereal disease and has not, according to regulations, had prophylactic treatment, he is court-martialed for disobedience of orders and, if convicted, is punished.

The weak point in regimental prophylaxis is the delay with which it is likely to be administered. To obviate this the use of established dispensaries under civil control has been urged for prophylactic stations. This has not been regarded with favor; partly because of the difficulty of enforcing proper discipline in such stations not under

military control, of carrying out the treatment with thoroughness according to regulations, and especially because of the obstacles in the way of assigning to nonmilitary bodies the carrying out of military regulations, for infraction of which the soldier may be called to account.

In order to meet this need for prophylaxis for soldiers when away from their stations a considerable number of "outpost" stations have been established. Where I have been able to get the opinion of commanding medical officers of divisions in which such stations exist, these "outposts" are useful.

In January, 1918, prophylactic "outposts" or City Early Treatment Stations for men exposed to venereal diseases were operating under the military control in the first 14 cities mentioned in Table 2. In the last 10 cities listed in this table preliminary plans have already been made (Jan. 25, 1918) to estabish similar "outposts."

Prophylactic packets to be given out to soldiers are not provided by the Army. They would undoubtedly be of some service, but their usefulness is diminished by the fact that such personal prophylaxis is regarded by the user as relieving him of the necessity for regimental prophylaxis, and experience has shown that the prophylaxis used by the individual himself is not as efficient as prophylactic treatment given under the eye of an experienced attendant. Perhaps the most important thing in prophylactic treatment is thoroughness in washing, and this will not ordinarily be carried out under the conditions in which personal prophylaxis is done. The soldier can buy a prophylactic packet if he desires; among the cases which would avail themselves of it, information is common about it and where it can be obtained. But it is not a part of the Army program; it is not carried in the Army supplies, and its use is not accepted as in any way a substitute for regulation prophylaxis.

TABLE 2

CITIES THAT MAINTAIN "OUTPOSTS" FOR THE EARLY TREATMENT OF SOLDIERS EXPOSED TO VENEREAL INFECTION

1. Ayer, Mass.	13. San Francisco (5)
2. Lowell, Mass.	14. Charlotte, N. C.
3. New York.	15. Fitchburg, Mass.
4. Brooklyn.	16. Baltimore.
5. Macon, Ga.	17. Atlanta, Ga.
6. Chattanooga, Tenn.	18. Louisville, Ky.
7. Boston.	19. Birmingham, Ala.
8. San Antonio, Texas.	20. Little Rock, Ark.
9. Hopewell, Va.	21. North Little Rock, Ark.
10. Petersburg, Va.	22. Spartanburg, S. C.
11. El Paso, Texas.	23. Greenville, S. C.
12. San Diego, Calif. (2)	24. Rockford, Ill.

Wherever I have been, there is invariable testimony to the value of medical prophylaxis. The number of cases of venereal infection

that develops after prophylaxis is surprisingly small. I have visited several regiments where no such cases had developed since mobilization. I have before me 2 division reports showing the relationship of prophylaxis to venereal diseases; these were taken quite at random. One shows that in the division there had been given during the week, 299 prophylactic treatments, which was presumably an average week; during the same week, no new venereal cases had developed after prophylaxis. The other covers the 12 weeks between November 3 and January 19, the leave of absence season. During this time in the division 1,706 prophylactic treatments were given; but only 18 cases of venereal disease developed after prophylaxis, and only 4 of these developed in patients to whom prophylaxis was given within 8 hours after exposure was said to have occurred.

Among the measures which are regarded as prophylactic must be included 2 others; one is the loss of pay which, according to army regulations, disability from venereal disease entails; the other is the fortnightly physical inspections. Both of these, in force since 1912 (Lyster), are regarded by Army authorities as very important measures in the reduction of venereal diseases.

MEDICAL CARE OF VENEREAL DISEASES

The second item in the medical program and the last item in the entire program is the medical care of those who are venereally infected. Necessarily the first step in putting into practical force the care of venereal diseases in the new Army was to obtain a group of competent specialists in their treatment. In going through the personnel of the medical reserve corps there was found a very considerable number of well trained specialists in genito-urinary, venereal and skin diseases. Among these were many of the best known men in the country in this field. The time of the great addition of soldiers to the Army was in September and October, when the National Guard and the National Army were mobilized in the 31 cantonments distributed over this country. Provision had suddenly to be made for the venereal care, as for the care of other diseases, of 31 cities, each containing a population of from 20,000-25,000 men between the ages of from 20-30 years.

It goes without saying that equally competent men were not obtainable for all these cantonments; but it can be said that at the time of the opening of each cantonment there was available in each, expert skill in venereal diseases. Since that time, as occasion has required, there

have been added to the various camps whatever men trained in venereal diseases were asked for by commanding officers or necessity seemed to require. Necessarily there was confusion and lack of preparedness in material ways at the time of mobilization in the cantonments; for one cannot build 31 cities in 3 months and at the end of the time have them as complete and finished as though they had existed always. The men in charge of venereal diseases, however, for the most part have shown themselves equal to the situation and the exceptions are few in which those affected with venereal disease have not been able to get adequate care in the cantonment base hospitals.

In the planning of the base hospital of each cantonment, full provision has been made for venereal diseases. It is a part of the policy of the Surgeon-General that acute venereal disease shall be confined to the hospital until the acute infectious stages are past. This means that all cases of acute gonorrhea belong in the hospital and all cases of syphilis which have early active lesions.

It is difficult at times to get this policy carried out. In many divisions the division surgeon has seen the wisdom of this course and has taken his own initiative in putting it into force. In a few places it has been for a time impossible, because the epidemics of acute diseases which have had prior demands on all of the available hospital beds. The policy has been thoroughly promulgated by the Surgeon-General and attention is called to it wherever neglect of it is discovered. This is, in some respects, a new military policy with us. It is one which it is believed will justify itself. It has several arguments for it; one is the great advantage which it affords in gonorrhea of curing quickly and preventing its spread to the posterior urethra; another is the assurance which it gives of thorough early treatment of syphilis, and the rapidity with which the infectious stage is passed; a third, and a very great advantage, is the reduction in the danger of nonvenereal spread of these diseases.

An effort has been made to standardize as far as possible the handling of venereal diseases. The first item of this consists in the hospitalization of acute cases, which has been referred to. There has been no effort to hamper mature men in carrying out established methods of treatment, but their attention has been called to the fact that, in the Army, team work is desirable, that bizarre and original methods are not necessarily most effective, and that the methods recommended have borne the test of experience. In carrying out this policy a small manual

of venereal disease has been issued which includes, in addition to the program of attack on venereal diseases, brief articles which represent present established methods of treatment of the various venereal diseases.

Hospital records are standardized as far as possible, and the effort is being made to carry this still further; so that, in addition to other advantages of standard records, there will be accumulated a large amount of information in the form of valuable statistical data on these diseases.

It is part of the program to provide in the base hospitals complete laboratory facilities for the care of venereal diseases. There is provided in each hospital a general laboratory in which Wassermann tests are to be made. It is also part of the Surgeon-General's policy that each venereal service in the base hospital shall have its own small laboratory equipped for examination for spirochetes and bacteria and for urinalysis examination. These laboratory facilities exist now in most of the cantonments that I have visited; in some they have not been developed. But wherever it is found that they are lacking, their establishment is stimulated.

In addition to the cantonments, there are many other large camps in which the care of venereal diseases is handled on the same plans as has been outlined for the cantonments.

It is part of the program to use the specialists in venereal disease in the division as instructors of other medical officers in venereal diseases. As a rule, the chief of a venereal service in a base hospital is the chief officer in venereal diseases. He is expected to be an instructor of other medical officers and his efficiency is partly gauged, not alone by the care which he gives his patients, but by the efficiency with which he develops his hospital organization, and the way in which he takes part in handling the venereal problem in the cantonment as a whole.

In order to increase efficiency in venereal diseases, 3 schools have been established for the intensive training of the less experienced men who are in this work. These schools are conducted by well known specialists in genito-urinary diseases and syphilis and skin diseases and are in centers furnishing large clinical material. The instruction furnished by these schools along with the experience that is being gained by the men in the venereal service of the various cantonments and camps, is, to say the least, keeping the men in this work from stagnating. There is little room for doubt that, in most instances, it is

increasing the knowledge of the junior officers rapidly. By this means, and by the constant addition of specialists from private life who are coming into the Medical Reserve Corps, it seems safe to believe that, as the demands on this service increase, we will be able to meet them with competent men.

The policy of handling the venereal diseases that I have outlined is that of the Surgeon-General, and, as far as it depends on central authority, it is efficiency carried out. Of course, the success of the medical care of venereal diseases varies greatly in the different cantonments. The organization of the Army, properly I think, gives large discretion to the division commander and similarly to the chief medical officer, who is the division surgeon.

The conduct of medical affairs in the cantonments, therefore, depends to a very large extent on the attitude of those in supreme authority; that is, (1) the commanding general in a cantonment; (2) the division surgeon, and (3) the commanding officer of the base hospital.

If either one of the first two, and the same is true to a less extent of the third, should be obstinate, opinionated and ignorant, and interfere, he could spoil the best efforts of competent chiefs of service under him. I know of no instance where this has been so flagrant as I have just indicated as possible, but I think it is true that there is considerable variations in the efficiency of venereal services due to variations in these commanding officers. Nevertheless, the efficiency of the venereal service is, in very large part, what the chief medical officer assigned to the service makes it. Some of the men taken from civil life are showing great originality and efficiency in this service.

To mention only a few of those whose work I have seen:

Major William W. Townsend at Camp Dix has developed a clinic in the base hospital that meets the most exacting requirements of what such a clinic should be.

Major J. Bayard Clark at Camp Lee showed the same sort of originality before he was called to similar work overseas.

Capt. Charles M. Williams at Camp Meade has approached the work from another side and has developed an original and most efficient system of looking after venereal diseases throughout the cantonment from division headquarters.

I mention these especially because they illustrate the fact that there is room for the personal equation, for initiative and originality. The

various intelligent plans which are developed are all useful additions to our experience in this work; and, partly on account of this fact, large latitude is given to the chiefs in the development of their services. The men previously mentioned undoubtedly could not have made such good showing without the support of their superior officers, but it is equally certain that with the same superior officers less efficient men would have made no such showing. One gains the impression, indeed, that in spite of so-called government red tape, military routine—which the civilian physician seems to regard in the way the public looks at medical etiquette—the equipment of the various hospitals, as well as their competency in other directions to take care of their patients, usually depends on the personnel of its medical officers. Sometimes it is impossible to get the necessary things, but as a rule you find the supplies ready for work in the place which is under the man who either knows how to get easily the things he needs, or is persistent enough to keep after these things until he obtains them, no matter how many obstacles he encounters in the endeavor.

QUALITY OF TREATMENT VENEREAL PATIENTS ARE RECEIVING

Venereal diseases are, as a whole, receiving excellent attention in the cantonment hospitals. Of course, the same factors of personal equation come in here, and the quality of service furnished in venereal diseases varies with the men who are furnishing it. But the men in charge of this work in the hospitals are trained specialists of long experience, and, without exception as far as my knowledge goes, are applying themselves with the utmost zeal and devotion to it. I have had a considerable opportunity to judge of the quality of treatment they are giving their patients and I believe it is as good as is to be obtained in any other 40 hospitals in the United States.

The place where patients with chronic gonorrhea and syphilis are likely to fail to get expert care is in the division as distinguished from the base hospital. The regimental surgeon must be a general practitioner while he is in that position. Adequate care of syphilis and of the chronic complications of gonorrhea eminently demand expert training, and this is not any more to be expected of the regimental surgeon than is special training in all of the other specialties. He also cannot have the special equipment necessary for it. It follows, therefore, that gonorrhea and syphilis should, as far as possible, be taken out of the care of the general medical officers. It is the policy of the Surgeon-

General to send them to the hospital as freely as practicable, and everything possible is done to encourage the return of ambulatory cases to the hospital for such treatment as they need. It is also the policy to have a qualified officer detailed to the special duty of supervising all venereal matters, including the treatment of venereal cases throughout the cantonment. But in spite of this, the fact remains that the weak point in the care of the soldier's venereal diseases is the care he receives when he is on duty; and he is allowed to stay on duty often when it would ultimately be better for him and for the service, if he were nominally as well as actually sick and under expert care. This is often due to the attitude of the commanding line officer. He wants his men or he does not want them, and he has no use for the soldier who is taking half-days off to go to the hospital for treatment. There is room for much education here, and for the development of considerable more cooperation.

RESULTS

The venereal situation in the United States Army has been excellent for several years. This is the result of the effective policy in handling these diseases that has been developed by the medical department. The present situation in the Army, then, as far as it is favorable, is not the result of any new policy, but is due to the continuation of the Regular Army policy, with such additions as the new situations have seemed to indicate.

Of course, a marked increase in venereal diseases was feared in the present military situation. Such an increase always follows mobilization of new troops, and the conditions which this great increase in troops entail.

Between 1897-1900, which was the period that covered the Spanish-American War, the venereal rate went up from an average of 80 per thousand to 160.

As Colonel Lyster says of our new Army, "higher rates will probably prevail for some time."

In order to appreciate the situation now, it is worth while to consider the Army record for venereal diseases for several years past: The venereal rate of the Army previous to 1898 averaged about from 80 to 85 per thousand. This is no criterion on which to base the comparison with present rates, for then we had none of the present means of diagnosis, and much that is now recorded as syphilis at that time

was not included. Colonel Lyster thinks under present conditions of recording syphilis, the rate for venereal diseases during that period would have been 110 per thousand or more. With the mobilization of new troops in the Spanish-American War in 1898 the rate suddenly doubled, going to 160 per thousand. The high rate then produced persisted after the War for 13 years, varying between 180 and 160 per thousand until 1911. Between 1909 and 1911, an effective policy of handling venereal diseases in the Army was developed by the medical department. The most important features of this policy were the enactment of regulations which provided for loss of pay for disability from venereal diseases, weekly physical inspections, and venereal prophylaxis. The result of this policy was shown by the rapid and continuous decline in venereal diseases. From a rate of 164 per thousand in 1911, it dropped to 116 in 1912, and by 1913, in 2 years, it had dropped to 86.

There are few more signal feats in sanitation than the reduction of 50% in venereal diseases in the United States Army, which was brought about by the policy of handling them developed by the medical department. This feat is the more creditable because it was the result of an original policy largely developed in our own Army and Navy.

Since 1913, the rate has remained under 90, excepting during 1916. In 1916, as a result of the rapid increase of the Army and the mobilization on the Mexican border, the rate went to 91.4.

In my estimates, I have taken the rate of 90 as the mean average toward which we should strive in the present crisis, although the rate of 91 in 1916 would certainly be fairly justifiable as the standard.

The rate for the Regular Army from September, 1917, to May, 1918, averages a little better than 90.

With the second week of mobilization in September, the venereal rate for the National Army shot up to 367 per thousand. The National Guard at this time showed a rate of 150. The Regular Army made a very strong showing for itself by presenting a rate of 80 on this particular date.

Much has been made of this enormous rate of venereal diseases at the mobilization of the National Army. As a matter of fact, it does not give any fair indication of the relative prevalence of venereal diseases in the 3 services, for this reason: When venereal disease is discovered for the first time in a soldier it goes on record and is counted as a new case. It may, however, be an old infection. The result is, when new recruits are received, all venereal diseases among them at

once enter the records; they include old as well as new cases. But after these old cases have once been counted, only actual new cases get into the records as new cases. It takes, therefore, about 4 weeks before the actual incidence of new cases of venereal disease in a body of troops can be determined. It does, however, give one a very fair idea of the relative prevalence of venereal disease in different bodies of troops to compare the rate when first recorded for these different bodies. And in this respect the contrast between the figures for the National Army and for the National Guard are interesting. The rate for the National Army for the first 4 weeks after mobilization of the Army was twice that of the National Guard.

I believe it may be said that fact shows that venereal disease was at the time of mobilization twice as common among the men who went in the National Army as it was in the men in the National Guard. That difference probably indicated what the relatively lax discipline of the National Guard could do in holding down the venereal diseases as compared with conditions of civil life where restraints are very much less in force.

During the months of September, October and November new recruits were constantly coming in, but their numbers were rapidly decreasing. From the time of mobilization, the venereal rate in the National Army showed a remarkably rapid decline. On December 1, these rates crossed below the rate of 90. From December 1 to date the rate for the National Guard has not reached 90 per thousand.

The rate for the whole United States Army for 1917, in spite of the enormous peak caused by mobilization, is 88, as compared with 91.3 for 1916.

It is interesting also to see what has happened with our expeditionary forces in France among whom the same general policy of handling the venereal problem is in force.

Among these troops we have none of the sudden peaks in our rate that occur when new troops first get into the records; therefore, we are able to obtain a fair idea of the normal rate of incidence of actual new cases of venereal diseases contracted while soldiers are in service. Since November 23, when the first report was published, to date for only 2 weeks has the venereal rate reached 90. The figures since December 21 are these: 75, 57, 74, 58, 52, 55, 44, 48. They are running almost nearly one half of what we might have expected as a reasonable showing when the war began.

7 West Madison Street.

DISCUSSION

Dr. W. T. Belfield: From 1906-1911 the average venereal incidence of the United States regular troops at home was about 150 men per thousand per year; that of the Prussian home army during the same period averaged about 19. Since the official adoption of the prophylactic treatment (1912) the venereal rate of our home Army has averaged about 90.

Prior to the present war the venereal rate in various foreign armies ranged about as follows: Italian, 77; British, 64; Russian, 63; Austrian, 54; French, 24; Japanese, 24; Prussian, 19; Bavarian, 17.

The United States Regular Army has, therefore, been distinguished for many years by a markedly higher venereal rate than that of any other army—a rate 4-6 times as high as that of the most efficient troops of Europe and Asia.

How shall this excessive rate be decreased? To elicit discussion I venture to offer certain suggestions, comprising educational, punitive and prophylactic measures.

A. *Educational.*—1. Our Army should learn the lesson so well taught by Japan and by Germany, namely, that in all matters concerning the health of troops the medical officers should have supreme control. It is perhaps to our credit that we are mere amateurs in the art of war; but it is less creditable that we are so slow to learn from experts. The medical officers of our Regular Army have always been regarded as poor relations, mere ministers to the sick and wounded; their equally valuable function—that of preventing preventable disease—is not exercised as it is in efficient military systems.

2. The soldier should be carefully instructed concerning the disasters, immediate and remote, wrought by venereal disease—this is already included in the Army program.

3. He should be informed that the comfortable doctrine current among men, which asserts that sexual indulgence is necessary for bodily health, is merely a flimsy pretext for self indulgence. For (omitting all other proofs) it is common knowledge that during 18 months' warfare with the Russians, 1904-1905, the Japanese troops maintained a standard of health never before equaled by any large army, Japanese or other; yet no prostitutes were allowed to mingle with these troops.

The fruits of such educational seed depends, of course, on the intelligence into which it is sown. Among over 3,000 male students of a certain state university the venereal rate was reduced through such education to one-tenth its former figure. Such happy effect from more instruction cannot be expected in those whose heredity and environment have been less fortunate; but all our soldiers should certainly have the information, however much or little profit they may derive from it.

B. *Punitive.*—It is notorious that in our Army venereal disease causes more disability from military duty than any other disease. If the present rate be maintained throughout the year over 150,000 men will be exempted from active duty for variable periods because of such disease. While the most serious disasters will redound to self, family and nation after their return to civil life, yet the immediate impairment of military efficiency is too serious a matter to be ignored. It is suggested that we follow the efficient German practice of making the acquisition of venereal disease a cause for punishment. The government need not forbid illicit sex relations; it may continue to minimize temptation and to use the prophylactic treatment; but if venereal disease result from the soldier's voluntary act, the childish plea—"Didn't know it was loaded"—will no longer avert punishment.

C. *Prophylactic.*—The excessive venereal rate of our Army—far greater than that of any other—seems due in large measure to the tardy use of the

prophylactic treatment. This measure appears to confer virtually complete immunity if properly used within an hour after exposure; it has often failed when used 4 or more hours thereafter. Under present regulations it is not used until the soldier returns to camp, an indefinite number of hours after exposure, depending largely on the length of his leave. Since he cannot be brought to treatment within an hour, it is obvious that the treatment should go with him—that he should be supplied with the protecting remedies and taught to use them immediately after exposure. This was, indeed, the method adopted when the prophylactic treatment was introduced into our Army in 1909—in a half-hearted, clandestine way, through confidential instructions to medical officers (because the authorities feared the criticism that they were encouraging immorality). It is not surprising that a measure introduced in this timid way, by medical officers devoid of authority to enforce it, should have been ignored by the ignorant soldier, and that it should have been supplanted by the present inefficient method.

It is suggested that either a complete kit—soap, protargol solution and calomel ointment—or at least soap, which alone destroys the spirochete of syphilis (Reasoner), be furnished each soldier; that he be taught how to use them properly; that he be ordered under penalty to use them immediately after exposure; and to report for the official treatment on return from leave. If the soap be scented with some freakish perfume and the calomel ointment colored with an aniline dye, his neglect to use either would probably be detected when he reports at camp for the official treatment, in which event he is penalized. If he fails to report exposure and develops venereal disease, he is penalized under present regulations.

It is rumored that the present inefficient use of the prophylactic treatment results from the pressure exerted on our military authorities by certain worthy people who oppose individual prophylaxis on the ground that it will encourage immorality. Many excellent people thought it better that a million children should die of diphtheria than that a thousand guinea-pigs should be sacrificed to save those children's lives; and some people still argue that the hideous mortality of our troops from typhoid fever in 1898 is preferable to the use of antityphoid inoculation. Even the inefficient prophylactic method now in use has cut the Army rate from 150 to 90; that is, for an Army of 2,000,000 men from 300,000 to 180,000 cases of venereal disease each year; by adopting the measures used abroad the number should be reduced below 60,000. It is theoretically possible that the adoption of individual prophylaxis may increase the number of exposures; it is certain that it would decrease the number of infections.

To summarize: The excessive venereal rate in our Regular Army, averaging 4-6 times that of efficiently managed armies abroad, seems to be due in part to 3 oversights:

1. To the medieval practice of regarding medical officers as mere ministers to the sick and wounded, ignoring their value in preventing preventable diseases (including venereal infection) when given authority so to do.

2. To delay in the use of the prophylactic treatment; because individual prophylaxis by the soldier himself is not used.

3. To the failure to proclaim the acquisition of venereal disease through a voluntary act as a punishable offense against the service.

That our government's firm and intelligent handling of the liquor question in the Army will confer extreme benefit on Army and nation, is obvious; it is to be hoped that this unique opportunity to confer even greater benefit through equally firm and intelligent handling of the venereal problem, will not be lost.

32 North State Street.

COMPULSORY NOTIFICATION OF VENEREAL DISEASES

REPORT OF THE COMMITTEE ON VENEREAL DISEASE OF THE INSTITUTE OF MEDICINE OF CHICAGO

On the question of notification, the Committee on Venereal Diseases makes the following report:

It believes that compulsory notification of venereal diseases at the present time is open to so many objections that it is undesirable and should not be attempted. The chief reasons for this view are as follows:

1. Notification of venereal diseases in the present state of public opinion is impractical.

2. The information obtained by attempts at compulsory notification is so incomplete as to be valueless.

3. Notification would serve no very useful purpose at the present time in the war which should be waged against venereal disease.

4. It would furnish a serious obstacle in carrying out the therapeutic attack on the venereal diseases, which is the first measure that should be undertaken against them.

1. Notification laws against the venereal diseases are impractical because in the present condition of public opinion they cannot be enforced. They are demanded by only a small part of the community, and they would be confronted by a very determined opposition from a very large part of the community whose private histories would be involved. Only the strongest public demand for the enforcement of such a law would make it effective. Until such a demand can be created, laws requiring notification would prove to be useless and would only serve to lower respect for legal regulation in public health matters. This is shown by the reports which are now made in this country in states and cities where notification of venereal diseases is compulsory. The following figures are taken from the state reports published in the reports of the United States Public Health Service covering the 11 months from Feb.-Nov., inclusive, 1915:

In Detroit (population over 500,000) from Nov., 1915-Nov., 1916, there were 83 cases of venereal diseases reported. In New York City (population 5,500,000) during the 8 months from May-Dec., 1916, there were 3,962 cases of gonorrhea and 13,757 cases of syphilis reported.

TABLE 1

STATISTICS REGARDING VENEREAL DISEASES TAKEN FROM STATE REPORTS

State	Approx. Popula.	Gonorrhea	Syphilis	Total
California	3,000,000	526	297	823
Kansas	1,800,000	54	41	95
Louisiana	1,800,000	90	60	150
Ohio	5,200,000	2,043	841	2,884
Vermont	360,000	343	1,749	2,092
Wisconsin	2,500,000	126	24	150

Since these reports were tabulated, later figures have been obtained from some of these states, but the results show no material difference.

The total unreliability of these records is shown by a glance at them. With the possible exception of statistics for syphilis for New York City, and we believe that this is not an exception, the statistics make it manifest that the venereal diseases are not reported; 823 cases for California in 10 months is surely less than the number of cases that occur in Los Angeles alone; 150 for Louisiana would not represent the number of cases in one of the larger towns; 95 for Kansas does not represent the total number that would be seen in 10 months by 2 or 3 physicians who had a large practice. And so the statistics go. It is probably within the facts to say that gonorrhea is 2 or 3 times as frequent as syphilis; yet the report from Vermont shows 343 cases of gonorrhea and 1,740 cases of syphilis reported. Most of the other state statistics show a larger number of cases of syphilis in proportion to gonorrhea than actually exist. The statistics for New York City show 13,752 cases of syphilis and only 3,962 cases of gonorrhea; that is, on the face of these statistics, syphilis would be 3 times as frequent in New York as gonorrhea. Of course, such a showing means inaccuracy; 4,000 cases of gonorrhea in 8 months in New York (500 cases a month) means that gonorrhea is not reported in New York.

2. Such statistics are, on the face of them, valueless. Nobody who knows the situation would regard them as throwing any light whatever on the prevalence of the venereal diseases, and no course of action concerning the venereal diseases could be based on them.

3. If it were practicable to quarantine or isolate venereal diseases, notification could be urged on that ground, but the extent of the venereal diseases is so great that measures restricting the liberty of the patients to any large extent are impractical. It is well within the facts to say that 20% of the male population have had venereal diseases, and that of this 20% a very considerable proportion have not been

cured. Quarantine regulations against 1 or 2 millions of the male population of the United States are economically impractical even if there would not exist a strong determination to oppose such a measure by the affected part of the community. And it must be remembered that this affected part of the community does not include simply the riff-raff—it includes all classes, not excepting the most influential.

It may also be pointed out that effective laws can be made for compelling patients to undergo treatment for venereal diseases without compelling notification of cases.

This is exemplified by the Health Act of Western Australia, under which patients are required, under heavy penalty, to seek treatment and to continue it until they can obtain a certificate of health from a qualified practitioner. Patients who do this will not be reported to the health authorities; all others are reported. This act, which is most drastic in its regulations, nevertheless does not require even anonymous notification.

It is often said that it is a necessary prerequisite to the sanitary attack on the venereal diseases, as of all other diseases, that the extent of these diseases should be known. This is a plausible statement which we believe analysis shows to be not true. The prerequisites to an effective intelligent sanitary attack on an infectious disease are: (1) to know the means of its transmission, and (2) to know the duration and the sources of infection in the infected. With yellow fever, for example, which is the most striking illustration, it was only necessary to know the duration of its infectiousness in yellow fever patients, and its means of transmission, to control the disease. With the venereal diseases also, we know all the facts necessary to their control.

There is no need for definite statistics to establish the wide prevalence of the venereal dieases, or their importance, and it is not a prerequisite to an intelligent attack on these diseases to first determine with mathematical accuracy their frequency.

4. It is generally recognized by authorities at the present time that the most effective measure that the state could enforce to reduce the ravages of the venereal diseases is the provision of general opportunities for the treatment of venereal diseases during their active course, to the end that the contagiousness of them may be quickly overcome and the danger of these patients to the community thus removed. This therapeutic attack on syphilis is now being generally agitated, and proposals for putting it into effect are being made by the best authori-

ties throughout the world. In this scheme for the therapeutic attack on syphilis, it is fundamental that treatment shall be made as unobjectionable to the patient as possible. It is exceedingly difficult—and this far over most of the world is impracticable — to compel patients to undergo treatment until they are cured. Until such compulsion can be enforced, the cooperation of the patient must be obtained. In order to get this, treatment must be made accessible, convenient and as free as possible from objectionable conditions. The most objectionable condition that can be put on the venereal patient is to expose him to the risk of making public his secret. The proposal, therefore, to compel notification of these diseases, is directly in opposition to the plan of therapeutic attack, and the requirement of notification would make any therapeutic attack ineffective until such time as treatment could be made by law compulsory. Compulsory notification would drive patients from hospitals and clinics; from responsible practitioners of medicine; and from all sources of treatment which would live up to the law; and would be a strong influence to make them go untreated, or send them to irresponsibles or incompetents. The determination of the more self-respecting classes to have secrecy as regards venereal diseases cannot be overestimated in considering this problem. We do not pretend to pass on the question as to whether these secrets should be protected. We are simply considering the fact that anything that increases the possibility of these secrets becoming known would act as a strong deterrent influence against patients seeking the treatment that they should have.

The course of responsible organizations throughout the world which have had to do with this subject support the views of your committee on the subject of notification. Thus the British Royal Commission on Venereal Diseases which was appointed in 1913 and made its report after more than two years exhaustive investigation, recommended against the notification of venereal diseases — even anonymous notification — its reasons being of the sort we have suggested above. In the summer of 1916, a vast system for providing universal treatment for venereal diseases throughout England and Wales was established by the Local Government Board of Great Britain. This plan does not require notification. In Germany, where the most rigorous measures to combat the venereal diseases have been enforced during the present war — measures which take no account of the liberty of the individual — notification is not required. Germany has long made the strongest

efforts to combat the venereal diseases, but has not seen fit to require notification. Norway and Denmark are, we believe, the only European states that try to have compulsory notification.

In the foregoing argument, we have had in mind complete notification, that is, reporting which gives the identity of the patient. The same objections which pertain to complete notification pertain to a less degree to anonymous notification, that is, notification which does not apparently disclose the identity of the patient. The great objection, however, to anonymous notification is that it serves practically no useful purpose. It can only purport to furnish statistics of the diseases, and under our social conditions the statistics furnished by anonymous notification would be utterly unreliable. They would give no adequate idea of the extent of prevalence of the venereal diseases, and whatever effect they would have on the public mind would be rather to minimize the importance of these diseases than to give an accurate impression of their importance.

It is on grounds such as the foregoing that your committee believes that attempts at compulsory notification of venereal diseases, whether complete or anonymous, are impracticable under our social conditions at the present time, and mischievous in their effects.

(Signed) WILLIAM ALLEN PUSEY,
WILLIAM T. BELFIELD,
HERMAN L. KRETSCHMER,
THOMAS J. WATKINS,
OLIVER S. ORMSBY.

JOHN H. LONG: TEACHER AND CHEMIST

Frank Burnett Dains
University of Kansas, Lawrence, Kan.

Nov. 15, 1918 *

John Harper Long, in honor of whose memory we are gathered together this evening, was born in Steubenville, Ohio, Dec. 26, 1856. Left an orphan by the death of his father, he made his home with an uncle at Olathe, Kansas.

Hence it is we find him entering the new, and at that time, the far west University of Kansas, as a freshman in 1873.

His initiation into the subject that was to be his life work did not begin until his sophomore year, and then it was through the medium of Barker's College Chemistry, together with that of Elliot and Storer, both famous books at that day.

The young student was fortunate in one way — in that he had the careful instruction of George E. Patrick, a graduate of Cornell University and a student while there of J. M. Crafts. He was an able and enthusiastic teacher, and in spite of the meager facilities, achieved remarkable success.

His own words give a picture of the college days:

> By the end of the sophomore year, spent in the south and east basement room of Fraser Hall, two of us had become so much enraptured by the subject of chemistry that we decided to become the first workers in the "chemical course" to begin with the next year. Frank Morgan and I began the junior year, September, 1875, as special students in chemistry. We were moved into the southwest basement room, and had the whole place to ourselves. Although the laboratory was nearly bare, we were proud enough of the situation. We had a distinct place in the university life and were not averse to having the fact recognized. We read Naquet's Organic Chemistry, and in French, too, with Patrick, and thus learned something of two subjects at the same time. Naquet was a standard book in those days, and we worked pretty hard over it, but gravimetric analysis, as in all American laboratories, was the strong feature of our work. The big Fresenius was, of course, the guide. No well-regulated laboratory could neglect this. I think it paid. This kind of work calls for a drill in accuracy not readily secured in any other way. How many hundreds of times have I been led to wish that the modern physiologic chemists, the aristocrats among the elect, might have a one or two year drill in this line of work.

The training he received was largely a textbook and laboratory one. As he himself remarks:

> I do not remember that we had any scientific journals beyond Silliman's *Journal*, the *American Chemist* and the *Boston Journal of Chemistry*. Of large general works or handbooks there were none that I recall. But Patrick spent

* Joint meeting with Chicago Section of American Chemical Society.

much of his small salary on chemical literature, and it is likely that everything that Morgan and I saw of this kind came from his private library. One book I well remember. Patrick came into the laboratory one day with a new German book, the leaves not all cut, and throwing it down on the table, remarked: "Here, boys, is the best thing yet written." It was a new edition, the third probably, of Lothar Meyer's Modernen Theorien der Chemie. It certainly made an impression on me.

The young student's undergraduate days, despite the primitive conditions, had been profitable. He had received not only a thorough and fundamental training, but in addition had learned to think for himself. His first publication, "A Method for Determining the Velocity of the Wind," appeared in the Transactions of the Kansas Academy of Science in 1877. Graduating with the degree of bachelor of science in the same year, Long determined to follow along the path that had proved so inviting in his undergraduate days. Graduate instruction in chemistry had barely made a beginning in America — Johns Hopkins was in its infancy — and where should he go but to the Mecca, toward which so many American footsteps had already turned, the land of Liebig and Wohler.

The great luminaries at this time in Germany were: Hofmann, Bunsen, Fittig and Lothar Meyer, and it is but natural that the young Kansas should seek the man whose book "On the Modern Theories of Chemistry" had so influenced his student days on Mt. Oread.

Hence we find him for two great years, student and friend of the genial, helpful, and wise Lothar von Meyer; and here he further developed his ideals for accurate scholarship and ability for research, which were to bear such golden fruit later.

During the Tübingen days four pieces of work were published: one, "On the Action of Alcoholic Potash on Bromoform," and a second on "The Action of Water Vapor on Ignited Wood Charcoal." The point sought for in these two short investigations was the determination of the relation to each other of the various gaseous products formed in the reaction. The third paper was on the "Electrical Conductivity of Some Salt Solutions," while the fourth investigation had the title, "On the Speed of Diffusion of Salt Solutions," and constituted the dissertation for the degree of doctor of science, which he received in 1879.

These latter were purely physico-chemical researches, and it is interesting to note that many of his later investigations, in far removed fields, were aided and rendered more valuable by the application of physical-chemical methods.

But an end had to come to these delightful but fruitful years, and in 1880 he returned to America. His choice of a life work was teaching, not only because it afforded a livelihood, but it offered greater promise for future study and research.

The year 1880-1881 was spent as assistant with W. O. Atwater in the laboratory of Wesleyan University, Middletown, Conn., a place which has afforded a temporary refuge to many an American chemist on his return from Europe. Here he gained his first experience and success in the classroom. A former colleague on the Northwestern faculty, Prof. H. S. White, the mathematician, was a pupil of Dr. Long in the Middletown days and remembers him especially as one of the best teachers in the college at that time.

In addition to the usual academic work of the chemical department, one of the early experiment stations in this country had been recently started at Wesleyan by Atwater, and I fancy that during much of his spare time the new instructor was making analyses of various kinds, among them the tedious nitrogen determination by the old soda-lime method. Atwater was one of the pioneers in agricultural and food chemistry in this country, and it was about this date that he began his famous investigation on the composition of fish and flesh foods. Later, Atwater and Rosa built a respiration calorimeter which in their hands, and now, under the direction of Benedict, has given such valuable results in the study of metabolism.

Possibly because Wesleyan was a Methodist college, Northwestern University sent there for an instructor in chemistry. At any rate, the fall of 1881 found Dr. Long occupying the chair of chemistry in the college of liberal arts at Evanston, and at the same time, giving instructions in inorganic chemistry in the medical school in Chicago. The next year he was transferred to the staff of the medical school, so that his full time could be devoted to the needs of the professional department.

His life work had now really begun, and for nearly 4 decades, John Harper Long occupied a unique and increasingly important position in the development of medical education, of chemistry and of science in Chicago.

In order to do justice to this man, let me take up somewhat in order — time forbids great details — his many-sided activities. First of all comes his service in education, for he was primarily a teacher, who spared no efforts to develop a systematic course of instruction adapted to the needs of the student in medicine, and whose

secret of success was his personal and constant interest both in the pupil and the science he represented.

From the days of Paracelsus, chemistry had been regarded as one of the fundamental subjects in the medical curriculum, and so we find in the development of medical schools in this country, some of the greatest names in early American science associated with the chair of chemistry.

Benjamin Rush, the signer of the Declaration of Independence and the pupil of Black of Edinburgh, was the first professor of chemistry in the University of Pennsylvania. Hare, a successor, was America's first great research chemist; Samuel Lathrop Mitchell of Columbia, with his ideas on nitrogen and nitric acid, gave impulse to Sir Humphrey Davy's vast discoveries. Silliman of Yale enlarged his laboratory for the medical students, although he remarks plaintively, "They were in their habits too familiar, and sometimes noisy and rude." Nathan Smith, the founder of medical colleges in New England, in an address at Dartmouth in 1813, had a prophetic vision of the rôle that chemistry would play in medicine.

Unfortunately, these men were exceptions, and most of the teaching was on a par with that of Aaron Dexter, of early Harvard fame, of whom Dr. Oliver Wendell Holmes told this tale:

The professor is lecturing.

> "This experiment, gentlemen, is one of remarkable brilliancy; as I touch the powder you see before me, with a drop of this fluid, it bursts into a sudden and brilliant flame"; which it most emphatically does not do as he makes the contact. "Gentlemen," he says, with a serene smile, "the experiment has failed, but the principle, gentlemen, the principle, remains as firm as the everlasting hills."

This represents only too forcibly the condition of chemistry in the medical schools 40 years ago; the principle might be as firm (and as arid) as the everlasting hills, but the practice was lamentable, despite the rapid developments in medicine proper and the growing appreciation of the part that chemistry must play in its further advance.

Long's own views on this subject were most ably set forth in a number of published articles and addresses. One especially interesting and valuable contribution on the history and teaching of chemistry in medical schools was his address as vice-president and chairman of the chemistry section, at the Denver Meeting of the American Association for the Advancement of Science. It was reprinted in *Science* in 1901. Let me quote from a portion of this article, because it represents not only the status of medical education as he found it, but also indicates a partial remedy.

The American boy has been taught to hold practical things in the highest esteem, and chemistry was not practical. Professors and students alike felt it, and it is hard to tell who was the most to blame for the warped and stunted conception of chemistry held even at the present time by the great majority of medical men in this country. It is likely that much of the fault lay in the weak and wholly unsatisfactory manner in which chemistry was presented for 50 years in most of our medical schools. The professor of chemistry was usually a physician, who, as a rule, was not considered sufficiently strong to fill the chair of practice, obstetrics or surgery, but who might teach acceptably the less important branch of chemistry. For the convenience of such teachers a peculiar system of chemistry called "medical chemistry" was developed, and in some places persists to the present time. The idea that a man trained outside a medical school could teach the kind of chemistry which medical students really needed was of slow development in the United States, and in some quarters fails yet of recognition. But for part of the trouble we must go further back. While students in general courses were taught the elements of the sciences, languages and mathematics, by recitations and quizzes, medical students, with far weaker preliminary training, were supposed to be able to absorb the essential facts of a great department of human knowledge from lectures alone. The lecture system is responsible for much of the superficiality of the old-fashioned medical schools, and no real progress was made until it began to be recognized that a medical student must be taught as other students are. With the gradual dawn of this notion it became finally possible to introduce into medical colleges rational chemical instruction, and the laughable farce of presenting the so-called medical chemistry to students ignorant of general chemistry will in time be a thing of the past.

One of the criticisms made in this article had been answered for him when he came to the medical school, since it is to the lasting credit of the far-seeing and scholarly men who founded the Chicago Medical College — the medical department of Northwestern University — that they not only put a layman, trained only in pure chemistry, into this important chair, but they gave him an appreciative and enthusiastic support, which made his future success possible. The second criticism, regarding the type of instruction, Dr. Long himself solved in time. His greatest task when he began his life work in Chicago was to develop the material needs and methods for teaching, a task which he fulfilled most ably. The greatest handicap toward realizing his ideals in teaching was lack of sufficient room, so while the old laboratories on 26th Street served their purpose faithfully and well, it was a great advance when the new building at 2421 Dearborn Street was dedicated. When it was built these laboratories were the most spacious and best equipped of any medical school in the country.

His method of instruction consisted of lucid, well illustrated lectures, combined with adequate recitation and carefully chosen laboratory work. He realized, as shown by the previous quotation, the absolute importance and need of a thorough training in general and

analytical chemistry before discussing its application to medicine—a necessity not always appreciated until later, by certain eager students, who regarded a hasty test for sugar or albumin as the highest chemical ideal that a practitioner needed to realize. The analytical work was largely volumetric analysis. A wise choice, since it involves a knowledge of general reactions, demands a good technic, and is, in addition, especially helpful to the future clinician.

To satisfy urgent needs, as an aid in his teaching, he wrote a series of textbooks covering the fields of general chemistry, qualitative and volumetric analysis, urinalysis, and physiological chemistry. They were developed where possible along historical lines and were scholarly, scientific, and eminently practical, in the best sense of the word.

In succeeding editions were embodied the newer theories and advances in chemistry. Probably his most successful book was his "Physiological Chemistry," because, due to environment, Long turned his attention to that field which offered such vital problems, whose solution taxed every resource of the most carefully trained chemist.

In short, he was a great teacher, and the generations of students who sat under "Johnny Long" learned not only good chemistry, but accuracy, honesty, and an appreciation of the vital relation of chemistry to the profession they were entering, and a proper perspective regarding the same. His influence insensibly grew, so that few men have done more in their lifetime to raise the standards of medical education along chemical lines than Dr. Long.

From the 37 years of teaching medical classes, the nature of his major researches in chemistry, and of his official and unofficial relations with the teachers of medicine in Chicago, you can see how closely a great part of his life was bound up with that profession, and I know how keenly he appreciated the honor of an election to the presidency of the Institute of Medicine, not for personal reasons, but because he felt that it was a sincere recognition of the aims for which he had striven.

While I have placed emphasis on his work in the school of medicine, it should be remembered that for a time the dental students were in his classes, and for a longer period, the chemistry in the school of pharmacy was in his charge; and in these professional courses, the same careful instruction was given as to the future physicians. As a matter of fact, Dr. Long was dean of the school of pharmacy in the later years, before the present merger was made. It was a position

that he filled most ably, but not one that would have been predicted for him by some of his early colleagues in that school.

His services to that profession were very real not only in the training and standards he insisted on for the future pharmacists, but also in other ways—as a member of the Council on Pharmacy and Chemistry of the American Medical Association.

Let me turn now to other phases of his activities, which were as properly a part of his daily life and university services, as his rôle in the classroom.

One of the features of the academic life is the opportunity for "research" and a characteristic of Long is that the inspiration developed in his undergraduate and Tübingen days "to search for new truths" never failed him.

As an investigator and research chemist he achieved notable results, over 100 papers coming from his laboratories, despite the burden of teaching and other allied scientific interests. Time allows us, however, to indicate only the general lines of his work.

1. His first papers were in Analytical Chemistry — one on "The Determination of Thallium," and others, for instance, on the use of phenolphthalein as an indicator, the determination of fats, etc.

2. He published several researches on the optical rotation of organic compounds. This subject in which he was especially interested, doubtless led to the translation of Landolt's volume on the "Rotating Power of Organic Substances and Its Practical Application," which appeared in 1902.

3. Associated with this work were his studies on the inversion of sugar with metallic salts, and the speed of reduction of ferric alum by means of sugar.

4. From 1891-1896 appeared several publications on the precipitation of antimony from solutions of potassium antimony tartrate by means of sodium carbonate, sodium phosphate, sodium acetate or sodium thiosulphate.

5. From 1900 on, Long's investigations have to do almost solely with bio-chemistry. These can be summarized as follows:

(*a*) On Urine:

The estimation of urine. Analysis of urine composites; the relation of the solids present to its electrical conductivity, the definition of normal urine, etc.

(*b*) Casein:

Its rotation, salts, combinations with acids, hydrolysis, and some phenomena observed in its peptic digestion.

(*c*) Then followed several papers on the nature of feces fat and on lecithin.

(*d*) His most important and valuable investigations, both in quantity and quality, were carried on in the last 4 years, and related to the action of digestive ferments, with special reference to those of the pancreas.

Let me quote the titles of some of these papers, since in that way the scope of the work will be more clearly indicated:

"The Mutual Action of Certain Digestive Ferments."

"On the Digestive Action and Composition of Different Portions of the Pancreas."

"The Reaction of the Pancreas and Other Organs."

"Assumed Destruction of Trypsin by Pepsin and Acid."

"Optimum Reaction in Tryptic Digestion."

"The Normal Reaction of the Intestinal Tract."

Five papers were published in 1917 in the *Journal of the American Chemical Society*, showing how little the years had affected his productivity, until his last illness closed down on him.

As an act of justice it is fitting here to mention the names of the co-authors who so faithfully assisted in some of these later publications. They are as follows:

Frank Gephart,
W. O. Johnson,
H. A. Nelson,
F. Fenger,
H. V. Atkinson,
Miss Mary Hull,
G. W. Muhlman.

Let me turn now to Dr. Long's relation to outside interests.

He was for a long period a consulting chemist for the State Board of Health of Illinois, and the Board of Health of Chicago. This led to his connection, for nearly 20 years, with the great question which directly affected the future of Chicago — that of sewage disposal. So far as Chicago was concerned, she settled it by building the drainage canal, thus sweeping the whole mass of waste material down to the Mississippi. St. Louis and other communities, fearing for their water supplies, brought suit against the drainage board, to prevent such a diversion of the sewage; the case being known as Missouri vs. Illinois and the Sanitary District of Chicago. During these years thousands of analyses were made in the laboratories of the medical school of samples at every point from Lake Michigan to St. Louis, and it was conclusively shown that the sewage was oxidized so quickly in the running stream, that no such contamination as was feared could occur.

Dr. Long was really the chemical adviser for the State of Illinois and the Sanitary District. Mr. James Todd, the leading counsel on the side of the defendants, makes this remark regarding Professor Long's method of testimony on the stand:

> He was always in possession of complete composure. It was impossible to disturb him or to involve him in apparent, though not real, contradictions. He met questions propounded to him from a sensible as well as a scientific point of view, and met them squarely, with exceeding vigor. It was dangerous to cross-examine him.

The decision in the Supreme Court was handed down on Feb. 19, 1906. It was Dr. Long's testimony on the chemical problems of the case, based on his years of accurate, painstaking investigations on the destruction of sewage in running streams and the consequent self-purification of the river waters, that carried conviction on those problems. Professor Long always felt that this verdict was one of the great accomplishments of his life, since rarely has the future of a great community been so vitally affected and assured by a decision based so largely on scientific work.

Long's experience in analytical work (for instance, he was referee for the purchases of the Indian Board for many years) and his reputation as a physiological chemist led to his interesting connection with the question of food preservatives and food adulterations. Ten years ago, the government appointed a committee consisting of Remsen, Chittenden, Long, Taylor and Herter to conduct an investigation on the "influence of sodium benzoate on the nutrition and health of man," which was intended to be a check of the findings of Dr. Wiley and the Bureau of Agriculture in the same field. One series of experiments with a squad of 6 men was carried out in the Northwestern laboratories under the direction of Long. His own portion of the report covered 268 pages, and recorded an enormous amount of detail and numberless analyses.

The results while negative in respect to evil results were absolutely reliable and dependable, so far as this series of experiments were concerned.

Under the auspices of the same committee—"the Remsen Board"—two other researches were carried out by Dr. Long, both involving a dietary squad with the corresponding maze of data and computations. One was "an investigation on the effect of foods containing copper compounds on the general health and metabolism of man"; and the

other an analogous one on "alum in foods." In addition, his name is appended to two other reports of the Board: one "on saccharin," and the other on the use of "sulphurous acid" as a food preservative.

This work was prolonged through several years, and it may be said that Dr. Long's very extensive, definite and scholarly contributions to the question of food preservatives and food adulterations was of great value in the later administration of the "Food and Drugs Act."

It would have been natural, on account of Dr. Long's position and standing, that he should have been called on frequently to assist in medicolegal cases. I am inclined to think, however, that he refused consistently to take up this class of work.

During the years I was associated with him, the only case, so far as I know, in which he played an active part, was the famous Luetgart one. The trial, which excited great attention at the time, was a famous one on account of the mass of irrelevant scientific evidence introduced. The most interesting phase of this case from a chemical view were the trials carried on in the basement of the old soap factory, to see whether a human body could be destroyed by boiling in a vat of lye. The results showed, however, that the corpus delicti would be much in evidence at the close of the experiment, and not at all in the condition assumed by the state at the time.

Let me turn now to Long's relation to one of the organizations which has met this evening to do honor to his memory.

His membership in the American Chemical Society covers a quarter of a century. The year in which he joined was signaled by a congress on chemistry, held Aug. 3, 1893, in conjunction with the World's Columbian Exposition. Long was active in all of the arrangements for the meeting, and in chemical matters relating to the fair. It may be of interest to note that among the chemists who registered at this meeting and at the one 25 years later in Cleveland, were the following:

C. L. Parsons,
W. A. Noyes,
Arthur Comey,
C. F. Mabery,
William Brady of this section,
Charles H. Herty,
F. B. Dains.

Had he lived, Dr. Long's name would have been added to this list; for few members of the society have been more faithful than he in attendance.

Long realized the value of such meetings, and also the need for some sort of definite organization of the chemists in and about Chicago,

which would afford men with common interests an opportunity for meeting and becoming better acquainted. As a result due almost entirely to his initiative, the charter of the Chicago section was granted March 15, 1895.

At a meeting held June 3 in the lecture room of the Northwestern School of Medicine and Pharmacy, the Chicago section of the American Chemical Society was organized, with the following officers:

Frank Julian	President
J. C. Foye	Vice President
F. B. Dains	Secretary
J. H. Long	Treasurer

Only the speaker is left of this list, and of the 40 members who constituted the section at its beginning, few are now on the Chicago rolls.

The early meetings were held in the lecture room of the medical school, and were attended by a few faithful souls; but later, when a meeting place was chosen in the loop district where refreshments of various kinds could be obtained, the local interest in chemistry was appreciably stimulated.

During these early days it was mainly Dr. Long's energy and interest, his acquaintance with the technical chemists of Chicago and with the society at large, that kept the young section going. Later, when the University of Chicago men joined the society and the number of chemists in and about Chicago increased, the law of mass action came into effect, promoting its rapid growth. There is no better illustration of the rapid development of chemistry in this country than the increase of membership of this section from 40 to almost 20 times that number, and I am sure that no one rejoiced more in the growth of the Chicago section and what it meant in terms of chemistry, than its founder.

Long's abilities were early recognized by the men influential in the American Chemical Society. From 1895 until his death, he was a member of the committee on papers and publications; a post onerous and important, when it came to decisions regarding the policy of the journal and the quality of the matter offered for publication. At various times, he was also a member or chairman of other important committees.

The American Chemical Society honored itself and Long by electing him president of that society for the year 1903. It was a very

sincere and merited appreciation of his services to the society and his standing among American chemists. His presidential address delivered at the St. Louis meeting was a discussion of "Some Problems in Fermentation." Special reference was made in it to its relation to sanitation in the self-purification of streams by the bacterial oxidation of sewage.

A constant attendant, whenever possible, at the meetings of the American Chemical Society, his name will be associated with its growth, and his wise councils will be sadly missed.

Most of you here this evening were acquainted with Long and many know him intimately through years of intercourse. As a student, he had the reputation of being serious and hard-working, but at the same time, he entered into the lighter undergraduate affairs, as he did in social life in later years. He was a fast friend, genial, and had a keen sense of humor, which is an American's great asset. His interests were many sided, and that, coupled with his capacity for work, enabled him to achieve success in so many lines and to accomplish so much. Modest and unassuming himself, he was a hater of cant, pretension and slovenly scientific work.

A man of strong convictions, the result of accurate, logical thinking, he was, however, not dogmatic, but was willing to change his views on the presentation of proper evidence; but for what he believed to be right he was a good fighter to the last trench.

As a scientific man he was rigidly accurate and dependable, and his conclusions were based on all the evidence that could be brought to bear on the problem under investigation. He was conservative; but with that best kind of conservatism that is ready to accept new views, when they become matters of fact, and not mere speculation.

Of his home life we will not speak, except to say that it could not have been more ideal.

His last years were overshadowed by this terrific war, which he felt most keenly. My last conversation with Dr. Long, at the Boston meeting a year ago, was on that subject. He told me then that when a boy he had been offered an appointment to the Naval Academy at Annapolis, and that he regretted sometimes that he had not taken it. I can well imagine him as an admiral of the fleet, upholding, as he would, all the best traditions of the American Navy. Though he was unable himself to take an active part, except in council and spirit, in this world struggle for righteousness and democracy, two sons and a

son-in-law wear the uniform of his country. I would that he might have known of the splendid heroism of his son, Lothar, a lieutenant (now a captain) in the Marine Corps, who won unforgetable laurels in the terrific fighting about Chateau Thierry; and that he might have seen the end of this conflict, regarding which his faith never wavered.

I regret that my pen could not have done greater justice to my friend and former colleague, but of him are true, even to a greater degree, the words that he wrote in an obituary of Lothar von Meyer:

> "All who knew him mourn his loss as a man; chemists alone are able to recognize the loss to science."

November 15, 1918.

CHEMISTRY AND MEDICINE

A TRIBUTE TO THE MEMORY OF JOHN HARPER LONG

JULIUS STIEGLITZ
N v. 15, 1918 *

Dr. Long's life and work, so ably portrayed by Professor Dains, are an eminent instance of the value of the work which lies in the great field of effort resulting from the relations of chemistry to medicine. For many years the main subjects of his investigatitons were enzymic action and problems of nutrition, researches of equal interest and importance to the progress of medicine and to the advancement of chemical knowledge. No less close and vital were these relations in the important spheres of influence which Dr. Long had created about himself outside of his laboratory, as instanced by his service of 20 years on the Illinois State Board of Health and by his connection with the Council on Pharmacy and Chemistry of the American Medical Association from its inception in 1905 to the end of his life. The same breadth of interest, supported by his great ability and fearless honesty, led to his selection as a member of Dr. Remsen's famous Referee Board, and in the last year of his life also to his election to the presidency of the Institute of Medicine of Chicago, which was founded in large measure to further the cause of medicine through the stimulation of research in all fields contributing to the advancement of medical knowledge.

Dr. Dains has discussed in an admirable fashion the details of Professor Long's valuable contributions to science and to the cause of humanity, and I have felt that I could pay no truer tribute to the high aims and achievements of my life-long colleague and friend than by attempting to outline tonight some of the important features of the relations between chemistry and medicine and thus help to have the cause "carried on" which Dr. Long had so greatly at heart and had so nobly served.

From its earliest beginnings chemistry has found in medicine one of its greatest sources of inspiration; indeed, the very name of our science refers to the dawn of chemical knowledge in the temples of Egypt, the "land of Chêmi," where priests prepared simple remedies and studied their chemical nature. This close connection persisted through the centuries and found perhaps its crowning culmination in

* Joint meeting with Chicago Section of American Chemical Society.

John Harper Long, 1856-1918

the persons of two modern giants of the medical world: the greater one, Louis Pasteur, the chemist, who, turning to medicine and using his chemical knowledge and its exact criteria in its service, founded the knowledge of disease through microscopic organisms, the very foundation stone of modern medicine; and the second, Paul Ehrlich, who inaugurated the present most promising era of combating these dread causes of disease by the development of specific remedies, produced artificially in the chemical laboratory in the form of pure chemical compounds.

Between these two extremes, the cause of disease and its cure, chemistry has found such an infinite variety of lines of effort in contributing to medical knowledge that I must necessarily limit my subject and I shall do so by confining myself in large measure to those phases of it with which I am personally most familiar. How necessary such a limitation must be is no better shown than by the fact that at the present moment medical science seems to be turning to chemistry more and more as an essential factor in every one of its fundamental branches. That chemistry was essential in bio-chemistry and in physiology has long been well understood, but of recent years pathology also has turned to chemistry for the solution of its most important problems; the best preparation for a bacteriologist, I am told, is long and advanced training in chemistry; even the great science of zoology, so long held in thrall by the obvious fact of form, has now turned to chemistry. How vital these applications of our science are, has been impressed most insistently, perhaps, on me by the fact that some biologists seem at length to have reached the conclusion that those most important of all factors in human life, in the very evolution of our race, the factors included in the collective name of heredity, must owe their wonderful specific power of transmission of characters and character in final instance to the chemical nature, the specific chemical character of chemical molecules.

With this glimpse into the vast vistas of present and future developments in the domain of the relations of chemistry to medicine, I must turn from these most alluring questions and ask what my own chosen field of chemistry, which for the lack of a better name we still call pure chemistry, can contribute to the cause of medicine. Let me say at once that I speak almost on the defensive, I have been asked so often by eminent physicians, by physiologists and biologists of every kind, why chemistry is so intolerably slow and backward in solving what are quite obviously chemical problems — problems striking at

the very root of our health and happiness. The answer very simply is this: Pure chemistry aims to be and is an exact science; indefinite mixtures of substances, such as our tissues and secretions represent, interest us, it is true, most deeply, but we can handle them successfully only to the extent that we can isolate from them pure principles for exhaustive, complete investigation, so complete that we do not rest until we have dissected the molecule of the pure compound, have put it together again, and thus have acquired first-hand knowledge of the exact function of each of its members. In the same way, systems that contain more variables than we can control rigorously, as rigorously as the mathematicians, the physicists and astronomers control their material, pure chemistry puts aside until such a time when our knowledge has advanced far enough to give us exact knowledge of each component in the system, to make possible a rigorous analysis of the whole system.

Every physician knows what medicine would be without dissection, without an exact knowledge of the structure and location of the organs and members of the body; every physician knows, too, how the functioning of the parts in the whole can be understood only by an accurate study first of the functioning of each organ and each member. Now, the scientific dissection and reconstruction of the molecules of important isolated principles is as a rule an extraordinarily difficult problem. Thus, it took Baeyer, perhaps the greatest organic chemist of his generation, some 14 years to determine what we call the structure of indigo, containing only some 30 atoms. But his success opened the way with the inevitableness of fate to one of man's great triumphs over nature; for with the knowledge of its structure, the key was gained for the successful synthesis of indigo and its artificial preparation on a large scale, releasing many acres of land for the growth of other important products for human use. It took altogether some 34 years to complete the campaign for the successful production of indigo, and at that the campaign was planned and conducted by some of the keenest minds in our science and sustained by the prospects of rich rewards in gold for the successful issue. Similar vital work was carried out with other important dyes, such as alizarin or turkey red, methylene blue and magenta.

I am emphasizing these facts, not only to illustrate the method of pure chemistry, but primarily to show what the successful issue of its efforts means. These and other dyes had been used commercially with an empirical knowledge during the many years that great inves-

tigators studied them from the point of view of chemistry as an exact science; but with the successful issue of their efforts in the profound analysis of the molecular structure of fundamental dyes, chemistry has gained for man supreme and practically unlimited power over the whole problem of color. It has made it possible for us to make at will a dye of any properties we may desire — fast dyes for any fabric; unstable, sensitive dyes for photography; dyes of any conceivable shade, fluorescing, if you please, with any desired hue. This instance of the power gained by chemistry has already proved to be of great value in medicine, by the development of stains to differentiate cells, micro-organisms and tissues of every variety.

The lesson of this conquest of the world of color by man would be wholly lost, if you did not carry from here the conviction that the methods which have scored so brilliant a success in one field are absolutely certain to be equally successful in conquering the greater world of bio-chemistry. The methods evidently are painfully slow. It took two generations to complete the conquest of color; would ten or twelve generations be too long for the supreme conquest of the chemistry of life? The campaign has already long been started and many a great victory is a promise of the complete triumph that must ultimately come. I shall attempt to outline for you three of the greatest problems which chemistry is facing in a titanic effort to invade and explore to its minutest parts Nature's most precious domain—life: The problem of the synthetic remedy; the problem of the specific remedy; and greatest of all, the problem of living matter.

A brief survey of the development of our power to produce and control local anesthesia may serve to illustrate the kind of service chemistry is trying to render medicine in the domain of the synthetic remedy. The discovery of the effect of cocain in removing by a simple local application all sense of pain where it has been applied, is, I believe, considered one of the great blessings of modern medicine, an aid to the surgeon, no less than a godsend to the patient. When cocain was first exploited, there were two serious drawbacks to its use; one, its great cost—it was said to be worth its weight in gold, which necessarily limited its employment; the other, its poisonous character, by reason of which there were occasional fatalities connected with its employment. The story of the exploration of the structure of the molecule of cocain, like that of indigo, is for the chemist a most thrilling and romantic tale; great chemists made advances, only to meet with ultimate defeat — exactly as great explorers did in the

investment of the secrets of the domain of the North Pole or of the heart of Africa — until finally the penetrating genius of Richard Willstaetter succeeded in reaching the great goal.

The results of these investigations are found not only in the fact that medicine has now a host of valuable substitutes for cocain, which have powerful anesthetic properties without dangerous secondary effects, but even more than the gain in materia medica is this: In the conquest of the world of color it was found that color is primarily due to certain specific groups of atoms in the molecules of dyes, or rather, vice versa, that specific combinations of a few atoms in the molecules of compounds give specific properties and functions to these compounds. This is, of course, really a fundamental law of chemistry revealed again in so complex a field as dyes. Now, exactly the same kind of specificity should be found in medicaments; that is, each specific function should be found to be the result of the presence of perfectly specific groups of atoms in the molecules of the medicaments. It is this application of the principles of pure chemistry which we can follow in the planned production of new and better local anesthetics and it is this application which points the way to one of the greatest lines of research for chemistry in the service of medicine — to determine by exhaustive investigation the peculiarities of atomic groups which will give the clean, physiologic effects which every physician would like to have at hand in the treatment of disease. The path would thus be eventually opened to a truly scientific materia medica. In the dyes we have been able to control secondary effects, such as stability or fluorescence, and we have every reason to believe that chemistry can accomplish the same results and avoid untoward secondary effects in the problem of obtaining specific physiologic effects.

The tremendous development of the production of so-called synthetic remedies is the visible manifestation of the application of chemistry to the kind of research I have outlined. A large part of this manufacture of synthetic drugs is, no doubt, of no permanent value, a far too large a portion is unquestionably even detrimental to the best interests of medicine as the result of claims that are, to say the least, too sanguine and often quite without an adequate basis of fact. Again the lure of gold is marring while stimulating this great effort in behalf of mankind; but that real progress has been made has been amply demonstrated by the situation in this country in the matter of synthetic drugs, resulting from our war with Germany;

this war has separated the wheat from the chaff and shown that there indeed are a number of drugs, invented by chemistry, which may be considered vital in the treatment of disease.

The second line of research in the application of these methods of chemistry to the problems of medicine, which should be emphasized, is that which has found its most convincing expression in Ehrlich's great work on salvarsan and neosalvarsan, now known to us by their American official names as arsphenamin and neoarsphenamin. This is the most convincing instance of the wonderful opportunities in developing the specific chemical agent, that will kill a specific invading germ without permanent injury to its host. Quinin was, I believe, the first specific of this kind, and it would seem that it would have been only a single, self-understood step from the use of a natural chemical compound to the development of synthetic chemicals for similar purposes; but it took an Ehrlich to take the first great and successful step in that direction. Ehrlich, like Pasteur, was a chemist before he became interested in medicine, and it is important to know that in developing arsphenamin he used all the resources of pure organic chemistry, his special field, changing the structure of the molecule he was developing here a little, there a little, putting an apparently slight but essential finishing touch here and there, just as a sculptor would handle his clay and his marble, until finally, after 605 preliminary studies the product needed to produce the desired effect was perfected. In arsphenamin the ordinary path of synthesis was abandoned, that is, the ordinary path of taking a natural product like indigo, cocain or atropin and finding out the secret of the constellation Nature had constructed. Ehrlich struck out to build his own cunning molecular contrivance to kill the invading germ without harm to the host, and he succeeded brilliantly.

For many other diseases due to bacterial invasion medicine is now using specific antitoxins and vaccines, manufactured in some host or medium by the germs themselves. With the curative agency we find inevitably substances poured into our systems which are not needed for the effect desired and which may indeed be harmful. For instance, a child unfortunate enough to have received a prophylactic dose of diphtheria antitoxin is exposed to the dangers of anaphylactic shock if later an actual attack of diphtheria develops and the treatment with antitoxin is indicated in an effort to save its life. Surely, physicians would prefer to use some pure specific, if chemistry could prepare one, equally efficient, equally potent. The effort to prepare such chemical

specifics has been blazed by the discovery of arsphenamin and invites untiring research efforts on the part of chemists. Some of the other synthetic drugs which have already been prepared are specifics, if not in the sense of completely curative agents, at least as alleviating remedies of the highest value. The demands for luminal for the relief of epileptics, which have come in since its importation was stopped by the war, have been pathetic in the extreme, and the gouty sufferer, on the other hand, has been grateful that almost without any delay American chemists were able to produce phenyl cinchoninic acid or atophan, which clears the system of the ache-producing uric acid.

We come now to the third and last field of effort of pure chemical research in the service of medicine which I should like to include in this short sketch — the study of the chemistry of life itself, of protoplasmic agencies and activities. Such a study is clearly so fundamental that it must ultimately give the world the rational basis both for preventive and for curative medicine. The problem obviously is a tremendous one that must be attacked by many workers from many sides, and it will take generations of toilers to complete the great undertaking. That complete knowledge will come no one can doubt who has followed the brilliant advances made in the last 60 years. At this time I can refer only to a very few phases of this slow but triumphant march of our science to the knowledge of the chemistry of life — a few phases which illustrate different lines of attack and which at the present moment hold out the greatest promise of success.

First, let me recall the fact that Pasteur's first great contribution to science, as a young chemist of 26, was the discovery in a study of the crystalline character of tartaric acid, that matter may be arranged in molecules in space in an unsymmetric fashion, yielding distinct forms, which have in the simplest cases the same relations to each other as my right hand bears to my left, and that shortly after, he made the remarkable discovery that living matter discriminates sharply between two such forms, which are identical in every particular except that the one is the optical image of the other. Thus, he found that dextro-tartaric acid is destroyed by ferments, levo-tartaric acid is not. It is of interest to mention, in passing, that this very discovery, arising out of pure chemical researches, was the fortunate incident in Pasteur's life that drew his attention to fermentation and opened the path to his great work on the germ theory of life and disease to which medicine owes its present strength.

The mode of atttack used by pure chemistry is to isolate pure compounds and study them exhaustively, both as to structure and as to their chemical activities. In attacking the problem of protoplasm we must isolate such of its components as we can, the materials it uses as food, the materials it excretes, and study each exhaustively. Thus, another great leader in this field, Emil Fischer, has laid the foundation of the chemistry of carbohydrates by his brilliant studies of the monosaccharids. How important these studies are for the science of protoplasmic activity is shown by the fact that of the 16 stereoisomeric aldehyd hexoses, differing only in the space arrangements of the atoms in their molecules, only three, d-glucose, d-mannose and d-galactose, are directly fermentable. Fischer, again, in his classic researches on the amino-acids and the polypeptids has been laying another broad and sure foundation for the study of the ultimate chemistry of the proteins. It is characteristic of the greatness and thoroughness — and the slowness — of the methods of chemistry that this study of the chemistry of proteins is growing in the same way that a magnificent monument would be erected. It is well known that every one of the beautiful cathedrals of Europe was constructed not in one generation and by one architect, but rather slowly grew as the product of the efforts of succeeding generations, of the genius of successive architects. We see now only the foundations of the monument of the chemistry of the proteins, laid with painstaking accuracy by workers in all countries; none of us will live to see the completion of the monument in all of its glory, but those who best understand the work have a supreme faith in the ultimate realization of their vision, and with it must come an insight into the nature of protoplasm and of life which no other study can hold out to us in like measure.

What a wealth of problems lies ready for the bold investigator! We may think of the isolation and exhaustive study of the active principles of the secretions of the internal glands, on whose presence in balanced proportions our healthy existence depends in so large a measure. Suprarenin or adrenalin has already been isolated by our American Abel and prepared artificially by the Germans—Stolz and Flaecher. The active principle of the thyroid gland has been isolated by E. C. Kendall of the Mayo Laboratories and found so potent, that an unbelievably minute amount injected into patients makes the difference between disease and health. Dr. McCollum is closing in on the secret of the active principles in our food commonly called the vitamins; should they prove to be organic and not vital mineral com-

ponents, a study of their chemical nature and the structure of their molecules would follow, and what a triumph for humanity if we could then produce them from waste products like coal-tar, and help out the fast decreasing ratio between supply and demand of dairy and similar products in crowded populations. You men of medicine do use organs of animals, ground or extracted, to make good a deficiency in this or that secretion in disease, but how much greater would your confidence in your therapy be if in place of mixtures of uncertain potency, pure chemical products were at your disposal. It is not so long since you used to employ your most important specific alkaloids in the same uncertain way, but what modern doctor would now hesitate in his choice between strychnin and nux vomica, atropin and belladonna, morphin and opium! Moreover, the isolation of the pure alkaloids by the chemist has put into your hands the swift weapon of intravenous injection and the same promise is held out for the pure isolated principles of glands.

Isolating and investigating pure principles of food, of excretion, of physiologic secretion, even to the point of the structure of their molecules, is a great and important task of pure chemistry, but it deals with only half of the great problem. Life is dynamic, it is material in action, and hence there is another great side to the problem of the chemistry of life, namely, the relations of the laws of chemical action to life. Every advance in our studies in physical chemistry, the branch of chemistry in which we study chemical dynamics, has found its important reflection, often its immediate reflection in its applications to life phenomena. Thus, the principle of the conservation of energy in chemical changes forms the basis of a large and vital part of the work on food values and their relation to proper sustenance. Then we have the applications of the laws of solutions and of the theory of ionization in the use of saline injections, in the problems of fertilization as studied by Loeb, in the study of the regulation of the heart-beat. We have the application of the laws of reversibility and equilibrium by Hill and by Emmerling to demonstrate the reversibility of enzymic action and thus to account in some measure for the synthetic processes of protoplasm, without which life would be impossible.

The investigation of the laws of catalysis or acceleration of action is another study fundamental for the understanding of life, for, as Oswald has said, our bodies are wonderfully controlled machines in respect to that fundamental factor of Nature, the time factor. I need not emphasize the significance of the time factor in medicine, for we

all know that health and disease are distinguished in no way more characteristically than by such time factors as heart-beat, respiration, rate of growth, rate of elimination, of decay. Our time-controlling devices are essentially the catalyzing enzymes and the investigation of their mode of action, of their production and control in the body belong to the most important ones in medicine. Such diseases of nutrition as gout and diabetes are most likely the result of abnormalities of enzyme supply.

How rapidly a discovery in physical chemistry may find its application in the study of life activities is well illustrated by this instance: Prof. Wilder D. Bancroft at Cornell University a few years ago made some extremely interesting observations connecting emulsions of oil in an aqueous medium with the presence of sodium and calcium oleates in the medium and their adsorption by surface films of the emulsion. By varying the ratios he could produce at will an emulsion of oil in the aqueous liquid or an emulsion of the water fluid in the oil. These genial observations were hardly published when Dr. Clowes of Buffalo applied their principles successfully to such problems as the clotting of blood, the coagulation of milk, the chemical fertilization of eggs — à la Loeb, and to anesthesia. This work is a brilliant instance of the rôle played by colloid chemistry, the chemistry of colloid dispersions, in life phenomena. Since the major part of our bodies is a complex aggregation of colloid systems, and since every particle of protoplasm is itself a colloid, the importance of this side of chemistry for the study of life phenomena cannot be overestimated.

It is evident therefore that all phases of physical chemistry as well as the analytic and synthetic sides of pure chemistry are finding vast fields of investigation for chemists in the domain of medicine and its fundamental sciences, fields drawing to themselves ever-increasing numbers of ardent workers. The friend and collaborator whose memory we are cherishing tonight was himself an indefatigable worker in this great cause, whose ultimate goal is a complete and masterful knowledge of the science of living matter. We can in no way pay greater tribute to his memory and devoted career than to pledge ourselves anew to continue our own modest efforts toward the upbuilding of this monumental undertaking of man's courage and genius, altho we all know that only future generations will see the glories of the completed monument.

ANNOUNCEMENTS

At the annual meeting of the Institute, Dec. 4, 1918, Julius Stieglitz, J. E. Doering and C. A. Elliott were elected governors for five years.

At the annual meeting of the board of governors, Hugh T. Patrick was elected president of the Institute, and E. O. Jordan, vice president. Frank Billings was elected chairman of the board of governors, Joseph A. Capps treasurer, and J. Gordon Wilson, secretary. J. B. Herrick is the acting treasurer in the absence of the treasurer on service.

The membership committee consists of T. J. Watkins, chairman, Robert J. Preble, Thomas L. Gilmer, C. D. Wescott and W. T. Belfield.

At the beginning of December seventy-eight fellows of the Institute were on active military duty.

NOTES ON THE EPIDEMIOLOGY OF INFLUENZA

Edwin O. Jordan

Feb. 21, 1919

The first extensive, well-described epidemic of influenza occurred in 1510. Those who are interested in parallels in human history will appreciate the comment of Theophilus Thompson in his well-known Annals of Influenza, published by the Sydenham Society in 1852: "The Sixteenth Century, the great transition period from feudal tyranny to liberty and order, was ushered in with much commotion of the elements, and marked with destructive pestilence." A seductive analogy is shown further, remembering the part played by the caterpillar tanks in the Great War, in Thompson's entry under the heading of "coincident phenomena" for the year 1510 where he includes "Great devastation by caterpillars in Germany."

Since 1510 epidemics of influenza have recurred at irregular intervals. In the 19th Century, epidemics are recorded in England in 1803, 1831, 1833, 1837, 1847-8, 1855, 1889-90. Those of 1831 and 1855 seem to have been considerably less extensive than the others. The last typical and widespread outbreak of influenza in the United States prior to 1918 occurred in the winter of 1889-90. This was relatively severe. According to S. W. Abbott,[1] "There was no epidemic of influenza during the entire period of registration since 1842, within the limits of Massachusetts, which could compare in intensity with that which prevailed in the winter of 1889-90." The present epidemic of 1918 has been incomparably more severe than that of 1890. The influenza deaths in Massachusetts in 1890 in a period of 50 days were placed at about 2,500; in 1918 the mortality was estimated to be six times as great (15,000); the population of the state had not doubled in the interval.

The mortality due to the pandemic of influenza throughout the United States will never be exactly known, but may be conservatively estimated for the whole country at not less than 600,000. This estimate is largely based on figures given by the U. S. Census Bureau of the number of reported deaths from influenza and pneumonia in a group of large cities. High as the total is, it apparently does not represent the full loss of life accompanying the epidemic. The total

[1] Twenty-First Ann. Rept. of State Bd. of Health of Mass., 1890, p. 327.

number of deaths reported from all causes has shown an increase greater than that accounted for by the reported influenza-pneumonia mortality. In other words, a considerable number of deaths undoubtedly attributable to the epidemic might be overlooked if reference is had simply to the recorded influenza-pneumonia figures.

In New York City the three weeks of highest influenza mortality in 1918 were those ending Nov. 2. During this period the reported influenza-pneumonia deaths were 13,851, and the total deaths from all causes 18,265, or, deducting the influenza-pneumonia component, a total death roll of 4,417. In the corresponding three weeks in 1917 the total deaths after the influenza-pneumonia deaths had been deducted, amounted to only 3,365. This excess in the 1918 deaths (1,052—about 30%) must undoubtedly in large part be laid at the door of the influenza. During September, 1918, and again after the middle of November the total deaths in New York were less than in the corresponding period in 1917. It is probably not far wrong to assume that the whole of the increase in the 1918 death rate was due to influenza, and that during the period referred to the actual influenza death rate should be increased by approximately 8%.

The Chicago figures for the three weeks of maximum prevalence are as follows:

TABLE 1

COMPARISON OF TOTAL DEATHS IN CHICAGO, OCT. 12-NOV. 2, 1917-1918

Total Deaths		Influenza and Pneumonia		Total Deaths Less Influenza-Pneumonia Component	
1917	1918	1917	1918	1917	1918
1,905	8,194	199	5,942	1,706	2,252

Taking the periods of maximum epidemic prevalence for comparison the following data are suggestive:

TABLE 2

COMPARATIVE DATA COVERING THE PERIOD OF MAXIMUM EPIDEMIC PREVALENCE

	Total Number of Deaths Less Influenza-Pneumonia Component		Deaths Not Recorded as Influenza-Pneumonia but Probably to be Attributed to Epidemic		Per Cent. of Reported Influenza-Pneumonia Deaths
	1917	1918	Number	Per Cent. Increase	
New York City (Oct. 5-Nov. 16).......	6,774	8,122	1,348	20	7
Chicago (Sept. 28-Nov. 9)............	3,449	4,020	571	17	7
Chicago recrudescence (Dec. 7-28)....	1,706	1,829	123	7	9
Philadelphia (October)...............	1,848	2,688	840	45	7
Baltimore (October)..................	752	1,160	408	54	12
New Haven (October)..................	154	199	45	30	8

The increase in death rate in New York City over and above that attributable to the influenza-pneumonia component is distributed among certain other reported causes of which the following are noteworthy: "Organic heart disease," "tuberculosis pulmonalis," "congenital debility and malformations." For the month of maximum influenza prevalence the figures are as recorded in Table 3.

TABLE 3

INCIDENCE OF INCREASED MORTALITY FROM OTHER DISEASES DURING PERIOD OF MAXIMUM INFLUENZA PREVALENCE

Reported Mortality During Month of October for	New York City		Philadelphia		Chicago	
	1917	1918	1917	1918	1917	1918
Organic heart disease	864	1,228	265	397	332	512
Tuberculosis pulmonalis	644	826	204	363	319	334
Congenital debility and malformations	362	515	107	249	175	225

It is evident that the deaths reported under organic heart disease are so greatly in excess during the influenza epidemic period that a part of these at least must be regarded as either primarily due to influenza infection or to an attack terminating a chronic process.

Deaths from tuberculosis have usually shown an increase during influenza epidemics. In London the weekly number of deaths reported from phthisis rose to double the average during the height of the 1889-90 epidemic. A similar altho less marked increase in tuberculosis has occurred in the latest outbreak. In New York City in 1918 during the two weeks of maximum epidemic mortality (Oct. 19-Nov. 2) the deaths reported from pulmonary tuberculosis numbered 430 as compared with 264 for the corresponding weeks of 1917.

The deaths reported in our three largest American cities under the heading "congenital debility and malformations" seem also from whatever reason to have been increased during the period of influenza prevalence.

The remarkable age incidence of influenza mortality stands out with especial clearness when the total deaths at various ages are compared with the deaths in the corresponding period of 1917.

Altho some observers have been inclined to attribute the relatively low mortality of the age groups 30-40 and above as compared with the high mortality of the 20-30 age group to an immunity supposed to have been acquired in the 1890-93 epidemic, it is evident that this is not the real explanation. To mention only one point, the age group 30-40, if this assumption were true, might be expected to have a lower

mortality than the nonimmune groups below 20, but the opposite is the case.

The fact that during the epidemic period many men in the age groups 20-30 and 30-40 were in army camps makes it plain that the true age incidence of influenza bears even more heavily on these two groups than indicated by the figures in Table 4.

TABLE 4

RATIO OF DEATHS FROM ALL CAUSES IN CHICAGO IN EACH AGE GROUP IN 1918 TO THE DEATHS FOR THE CORRESPONDING PERIODS IN 1917

	Week of Maximum Mortality (Crest)	Six Weeks of Maximum Mortality	Trough of Subsidence (2 Weeks) (Nov. 16-30)	Recrudescence (3 Weeks) (Dec. 7-28)
Under 1 year	2.3	1.7	1.0	1.1
1- 2 years	6.4	3.3	1.4	1.4
2- 5 years	6.9	3.6	1.5	1.8
5-10 years	5.8	3.3	1.1	1.5
10-20 years	8.8	4.8	1.3	2.2
20-30 years	15.5	9.4	2.3	2.9
30-40 years	9.2	6.5	1.8	2.5
40-50 years	3.5	2.3	1.3	1.5
50-60 years	2.0	1.6	1.2	1.3
60-70 years	1.9	1.6	1.0	1.4
70-80 years	1.5	1.2	1.0	0.8
Over 80 years	1.5	1.4	1.0	0.8

The sources and modes of infection in influenza are more likely to be determined by observations on small population groups than by studies on the course of the epidemic throughout the country or in large communities. The following observations emphasize the importance of prolonged contact in furthering infection.

In October, 1918, influenza broke out in a group of the Student Army Training Corps at the University of Chicago. This group, known as Section B, comprised 234 men, nearly all about 20-22 years of age, coming mostly from small cities, towns and rural districts in Illinois. They were housed in five different places — remodeled houses and apartment buildings. The number of occupants to a room varied somewhat, being usually about four to eight. Although sleeping in five separate buildings, they were all closely associated in their technical class work and at meals. The men for the most part came directly from their homes, arriving in Chicago October 15 and 16. Three of the men were ill on their arrival, in two cases with symptoms that as described seem influenza-like. On the evenings of October 16 and 17 all men in the group were brought into especially close contact in the locker room of the University gymnasium while waiting for their physical examination.

The date of onset was determined by individual questioning in each case and could usually be fixed by the patient within a few hours as is characteristic of influenza. The cases developed as follows:

Date of Onset	No. Cases	Date of Onset	No. Cases
October 15 } October 16 } (Ill on arrival in Chicago)	3	October 19	29
		October 20	22
		October 21	13
October 17	10	October 22	4
October 18	29	November 4	1
No definite information	9		

The situation became known to the University authorities on October 20 and all the affected men were removed to an emergency hospital.

Daily temperatures were taken of the rest of the group for one week. Isolation followed any sign of fever. The number of men in each building at the beginning of the outbreak and the corresponding number of cases is as follows:

Building	No. Men	No. Cases
A	15	5
B Upper	61	29
B Lower	30	11
C	19	4
E	40	17
F	51	16

In each of three buildings (Lower B, E and F — 121 men) one man was ill on arrival; in these houses 8 cases developed on October 17; in the remainder (A, Upper B and C: 95 men) with no known cases of illness before October 17, 2 cases developed on the 17th. In the later cases the time and place distribution did not give any indication that infection occurred principally in sleeping quarters.

The chief symptoms accompanying onset were (100 cases):

Headache	66
Muscle pains	56
Sore throat	37
Cough	34
Nosebleed	8

Fever ranging from 100-104 F. was present in all these cases. The face was usually deeply flushed and the conjunctiva more or less injected.

Information was obtained about previous illness in 87 cases. In eight instances there had been definite illness within a year: malaria, 3; measles, 2; rubella, 1; mumps, 1; bronchitis, 1. Prior to January, 1918, there had been in addition to the usual diseases of childhood:

typhoid, 5; scarlet fever, 4; diphtheria, 2; pneumonia, 6; "grippe," 3. In two cases tonsils had been removed. Two men gave a history of frequent colds in winter. In the group as a whole there was no evidence of respiratory tract ailments just prior to the outbreak.

Meals were served to these men in a separate building several blocks away from their dormitories. Mess-kits were not used. The food and general supervision were the same as for the rest of the student community including Section A of the S. A. T. C. The men had nothing to do with the washing of dishes and tableware, which are known to have been thoroughly cleansed in boiling water.

During the epidemic period another group (Section A) of the Student Army Training Corps were likewise under observation. The majority of this group (685) were housed in dormitories and fraternity buildings under conditions very similar to those obtaining in Section B. Their classrooms and eating places were entirely apart from those of Section B, and the men of the two groups came into no sort of formal contact with one another. The cases of influenza among 685 men in Section A occurred as follows:

Week Ending	Cases in Section A
October 5	7
October 12	10
October 19*	7
October 24	4
November 2	2
November 9	3

* Week of maximum prevalence in Chicago.

The number affected in the different dormitories used by Section A is as follows:

Section A

Dormitory	Approximate No. of Men	No. of Cases Influenza
H	215	14*
S	120	6
M D	50	4
N D	100	4
S D	100	3
P	100	2
	685	33†

* These cases developed on well-scattered dates between October 6 and November 8, never more than two in one day.
† Two of these cases developed pneumonia; there were no deaths.

In addition to this number there were 271 men of Section A living in barracks — half of this number after October 20, the other half after October 29; but two cases of influenza developed in this group, both on the same day (November 8). At the time these men entered

barracks influenza in Chicago had decreased considerably from the maximum. Beginning with the assembling of the students October 1 and throughout the epidemic period, special care was taken to detect cases of incipient illness. Frequent talks were given to men and officers and all men of Section A with any sign of illness, objective or subjective, were instructed to report to the medical officer, and whether "simple colds" or suspected influenza, were at once isolated in the hospitals or sent to their homes. During the whole period lectures and other classes were held as usual, one group of 350 men meeting three times a week.

The groups may be compared as follows:

	Section A	Section B
Number men	685	234
Cases influenza developing Oct. 17-22	2	92
Total cases influenza developing Oct. 17-Nov. 8	26	93*
Cases pneumonia	2	12
Deaths	0	2

* In 9 others the exact date of onset could not be ascertained.

The mode of housing was similar in the two groups; the food supply was under central supervision and the men themselves had nothing to do with its preparation or serving; neither group received any specific or mixed influenza vaccines. The cases of illness that developed in Section A were quickly isolated, whereas in Section B isolation was less early and much less complete.

Cessation of influenza in Section B followed immediately after the isolation of all cases and the inauguration of daily inspection. The natural immunity of the men of Section B who had not become infected before October 21 was undoubtedly relatively high.

A third group of students, men and women, not living in barracks nor for the most part in dormitories, but at their own homes or in boarding houses, gave the following record:

Number of students	82
Cases influenza	7
Cases pneumonia	1

The case incidence is here somewhat higher than in Section A, where the greater restrictions placed on individual movement unquestionably decreased the amount of contact with the civilian community. The general degree of health supervision was also less than in the Student Army Training Corps unit.

Comparison of these two groups (Section A and civilian students) with the heavily affected Section B, in which the case incidence was about six times as great, indicates the importance of early detection and isolation of influenza cases as a preventive measure.

THE BACTERIOLOGY OF INFLUENZA

David J. Davis

Feb. 21, 1919

A real contribution will have been made to bacteriology if the present epidemic enables us to determine the true relation of Pfeiffer's bacillus to influenza. Since Pfeiffer discovered his small hemophilic bacillus and stated that it caused this disease almost the entire medical world accepted his conclusion. By only a few investigators, and these chiefly among the French, was his statement called into question.

His classical article on "Die Ætiologie der Influenza" [1] is based on work done in 1892 in connection with a secondary and minor epidemic of so-called influenza. He merely states that he saw and photographed similar bacilli in smears 2 years before in the pandemic of 1889-90. His article is singularly free from statistical detail. He does not state how many cases he examined nor the percentages of positive and negative results by cultural methods. He uses general expressions such as "the bacilli were always found in sputum, etc." In his first brief communication[2] he states he examined 31 cases and found them in all. Evidently this statement is based on smear preparations and therefore untrustworthy since he had not as yet discovered his method of growing them on blood. The later work of that period by others is likewise unsatisfactory in respect to statistical detail and especially in control observations. Pfeiffer examined a few cases of bronchopneumonia and three times found similar bacilli. But they were somewhat larger and tended to form threads and he therefore called them pseudo-influenza bacilli. Such bacilli have later been shown by numerous workers to be identical with influenza bacilli. Pfeiffer's work was a splendid contribution to pure and technical bacteriology, but was weak as a study of the causal relationship of a germ to a disease.

Pfeiffer made so few control observations on other diseases at that time that he could not know of the very common occurrence of similar organisms in the sputum and exudates in nearly all respiratory infections and also often in normal throats. I have gathered my own data together in tabular form which I here present.

[1] Ztschr. f. Hyg. u. Infectionskr., 1892, 13, p. 357.
[2] Deutsch. med. Wchnschr., 1892, 18, p. 28.

The data here given should be comparable. In all the examinations blood-agar plates were used. For the most part human blood was added, but in many of the earlier examinations pigeon blood (following the suggestion of Pfeiffer) was employed. While in pure cultures pigeon blood yields a better growth than many other bloods the influenza bacillus growing in symbiosis with other bacteria, as is practically always the case in sputum and throat cultures, will do as well on the one as on the other. According to my experience this is true also of heated blood agar. The influenza bacilli were in each case isolated in pure culture and for identification were required to fulfil the following requirements: (1) a small, gram-negative, nonmotile,

TABLE 1

B. INFLUENZAE IN SPUTUM OR THROATS IN VARIOUS INFECTIOUS DISEASES

Disease	Number of Cases	B. Influenzae Present	Percentage Positive
Influenza epidemic, 1918	62	5	8
"Grippe" epidemic, 1905	17	3	17
"Grippe" epidemic, 1908	23	[illegible]	17
Bronchopneumonia, 1908	26	10	[illegible]
Lobar pneumonia, 1909	12	[illegible]	33
Pertussis	68	61	89
Measles	23	13	[illegible]
Tuberculosis	5	3	60
Varicella	11	7	[illegible]
Acute articular rheumatism	11	[illegible]	0
Meningococcus meningitis	11	[illegible]	36
Influenzal meningitis	7	7	100
Tonsil crypts	300	3	1
Normal throats	20	2	10

polar staining bacillus; (2) growth on medium containing hemoglobin; (3) symbiosis as revealed by profuse growth on blood-agar plates around a foreign colony. This property I regard the most important one of all and is absolutely diagnostic of B. influenzae. The hemoglobinophilic property is not distinctive, since several other organisms have been described possessing this characteristic. Smear preparations from the throat and sputum were often made but never relied on for purposes of identification. Examination of smears may suggest the presence of B. influenzae, but is quite untrustworthy.

It will be noted from the table that excluding influenza meningitis, influenza bacilli are most often found in pertussis. The "grippe" epidemics of 1905 and 1908 were more or less local outbreaks of infections that clinically were strikingly like influenza. They were, however, different from real influenza, particularly in their epidemiologic and pathologic aspects. Of the 62 cases of the present epidemic

(1918), the bacilli were found in 8%. These cases were nearly all typical hospital cases, and many of them had definite pneumonic symptoms. In 15 cases two examinations were made at intervals of a few days. In 42 the examination of the sputum was made in the 1st week, usually within the first 2-3 days. In 20 cases the examination was made after the 10th day of the disease. Twelve of the cases were from a second wave of the epidemic 1 month after the first which was typical clinically. In this the incidence of B. influenzae was not different from the first outbreak.

In certain diseases the incidence and the dominance of B. influenzae vary markedly in individual cases or in groups of individuals. In pertussis, in certain families where several cases appeared, the bacilli were found early and at times in large numbers in all infected members; in other families they might be rare or absent; or they might appear late in the course of the disease. There was observed one group of 10 children in a small hospital ward who, owing to cross infections, were suffering with both pertussis and measles. In every case the sputum, mouths and even the expectorated clear saliva were teeming with B. influenzae which could easily be isolated in almost pure culture on blood plates held before the patients several feet away when coughing. These cases were of average severity and ran courses in no way different from the ordinary. This was during an inter-epidemic influenza period. I have not seen any such striking predominance of B. influenzae in mouths during the present epidemic in a group or even in individual cases of influenza.

The reports of different investigators vary considerably as to the incidence of Pfeiffer bacilli in the present epidemic. Most workers find them in sputum in percentages varying roughly from 5-70%. In lung punctures and necropsy material from influenza pneumonia they have been found on the whole oftener than in sputum, the percentages of some observers reaching 80% or higher. Lord[8] found B. influenzae as predominant almost as commonly in interepidemic periods (25%) in acute and chronic respiratory disease as in influenza patients in the present epidemic (36%). Pfeiffer himself has not been able to find his bacillus with a high degree of constancy in this epidemic. It is interesting that the German and Swiss workers at the present time seemingly emphasize diplostreptococci more than Pfeiffer's bacillus. English reports, as I have followed them, lay

[8] Jour. Am. Med. Assn., 1919, 72, p. 188.

more stress on Pfeiffer's bacillus, and some attribute etiologic significance to it.

A few studies on the presence of specific antibodies in the blood following influenza have appeared. Fleming[4] has found agglutinins in moderate amounts. Rapoport[5] found that using an antigen composed of strains of B. influenzae recentllv isolated from lungs he obtained positive complement fixation in 54.5% of serums from convalescent influenza patients. His conclusion is that the results furnish no conclusive evidence of a primary etiologic rôle of the influenza bacillus. His studies thus far for the presence of agglutinins, opsonins and precipitins in the blood of patients have given negative results. These observations and some others made on specific antibodies in influenza serum tend to support the view that Pfeiffer's bacillus often plays a rôle in the disease, but not necessarily a primary one. The antibodies may have the same significance here as do the specific opsonins for streptococci found in scarlet fever.

Some time ago I[6] immunized animals against strains of influenza bacilli from measles, pertussis, varicella, conjunctivitis, tonsillitis, laryngitis and influenza. Serum agglutinins for homologous organisms appeared in dilutions of 1 : 500 and higher; for other strains in dilutions of 1 : 100-1 : 200. My own data do not point to either morphologic, cultural or specific differences between influenza bacilli found in these various infections. According to the observations of Wollstein,[7] in pertussis the serum will agglutinate homologous and other strains in dilutions of 1 : 50-1 : 100.

The pathogenicity of Pfeiffer's bacillus for man is unquestioned; witness the cases of meningitis[8] with pure cultures in the spinal fluid and heart blood and where mixed infection with other germs is excluded. In such patients there is nearly always bronchopneumonia with pure or nearly pure cultures of Pfeiffer bacilli present. This bronchopneumonia, however,[9] lacks many of the characteristics of the present influenza pneumonia. The experimental influenzal bronchopneumonia of Wollstein and Meltzer[10] by bronchial insufflation is also in accord with this statement, though they emphasize the tendency to hemorrhagic exudates. A large dose of B. influenzae from

[4] Lancet, 1919, 106, p. 138.
[5] Jour. Am. Med. Assn., 1907, 48, p. 1563.
[7] Jour. Exper. Med., 1905, 7, p. 335.
[8] Davis: Am. Jour. Dis. Child., 1911, 1, p. 249.
[9] Jour. Infect. Dis., 1912, 10, p. 259.
[10] Jour. Exper. Med., 1912, 16, p. 126.

pertussis when placed in the human throat by the writer[11] caused some fever and cough, and pharyngitis associated with a mucopurulent exudate lasting for a month in which at all times very large numbers of Pfeiffer's bacilli were seen and cultivated. True influenza was not produced. When injected under the human skin they cause swelling, redness and later suppuration, and will live for several days. They are, therefore, clearly pyogenic. The several experiments made recently in the military camps by inoculating influenza bacilli into the throats of volunteer soldiers have caused neither throat infections nor influenza.

In animals influenza has never been definitely produced by inoculation with the Pfeiffer bacillus. Large doses intraperitoneally or into the meninges, however, will kill rabbits, guinea-pigs, rats and monkeys with dissemination into the blood. When inoculated with cultures of staphylococci or other bacteria the virulence of both seem to be enhanced. This is probably a manifestation of symbiosis.[12]

I think then that the evidence at hand does not prove or even indicate that the influenza bacillus is the primary cause of the present epidemic or that it has ever been the cause of any epidemic. The reasons may be summarized as follows:

1. The influenza bacillus has not been constantly found in the disease in unselected cases by most observers. Even if it should be found and properly identified in 100% of cases this would not prove its causal relationship to influenza any more than finding 100% of hemolytic streptococci or the pneumococcus-like organisms would prove their causal connection to the disease.

2. It is found as commonly or more commonly in other diseases like pertussis.

3. Inoculation of human beings with Pfeiffer's bacillus has not caused the disease.

4. Animal inoculations have never reproduced it.

5. The influenza bacillus is pyogenic and causes leukocytosis. The primary blood picture in influenza is a leukopenia.

6. Influenza is a disease prone to secondary invasions. Pfeiffer's bacillus is known to be a common and early secondary invader in many respiratory diseases, and therefore we should expect to find it commonly in influenza.

[11] Jour. Infect. Dis., 1906, 3, p. 1.
[12] Jour. Infect. Dis., 1906, 3, p. 1.

7. Prophylactic influenza inoculations by Leary, Park, Rosenow and others have failed to reveal any appreciable protection against the disease.

8. There are as good reasons for saying the influenza bacillus is the cause of pertussis or measles as for saying it is the cause of influenza. Also, there are as good, perhaps better, reasons for saying the diplostreptococci cause influenza as for saying that Pfeiffer's bacillus causes it.

One may say, perhaps, that in spite of all the above points Pfeiffer's bacillus may cause influenza. In the face of these reasons, however, he who contends that it is the cause surely has the burden of proof.

As to other associated organisms in influenza, varieties of streptococci are important. According to my own observations hemolytic streptococci are not as numerous in the washed sputum early in the disease as they are in normal throats. In influenza patients under 10 days my figures are 31% positive and in few numbers; after 10 days 65% and more numerous often predominating. These observations are in accord with the findings of Nuzum[13] and his co-workers, Blanton and Irons[14] and others. In necropsies they are decidedly more frequent especially in empyema and late pneumonia when they appear to play an important rôle.

The so-called diplostreptococcus is perhaps the most important direct cause of influenza pneumonia and death. It is interesting that in the epidemic of 1889-90 these cocci were noted repeatedly and were seriously considered as the possible cause of influenza by Finkler,[15] Ribbert[16] and others before Pfeiffer discovered his bacillus. In the Swiss, German and English literature of the present epidemic it is repeatedly emphasized as being often found in the exudates, lungs and heart blood. Mathers in this country very early discovered this organism and clearly saw its significance, finding it in sputum, puncture fluids and blood. Nuzum, Hirsch and McKinney, Blanton and Irons and nearly every one working on influenza, have emphasized it. Some are inclined to view it as the causal organism in influenza, though most workers consider it an important secondary invader.

[13] Jour. Am. Med. Assn., 1918, 71, p. 1562.
[14] Jour. Am. Med. Assn., 1918, 71, p. 1988.
[15] Deut. med. Wchnschr., 1890, 16, p. 85
[16] Deut. med. Wchnschr., 1890, 16, p. 61.

These diplostreptococci seem to be chiefly pneumococci of types IV and II, though many strains are not easily classified, being irregular in their agglutination, bile solubility, and inulin fermentation. Some appear to belong in the Streptococcus viridans group as was true of Mathers streptococcus. Tunnicliffe[17] showed a specific variation in opsonins for these green-producing organisms in influenza and its pneumonia. Staphylococci and the M. catarrhalis are found occasionally, usually late in the course of the disease and no doubt are secondary agents. The consensus of opinion seems to be that all these organisms are secondary invaders.

What may be said concerning a possible primary cause? A number of organisms or agents have been announced as the cause, most of them by European investigators, but none I think deserve serious consideration at this time except the so-called filtrable viruses. The experiments bearing on this subject may be readily divided into two groups, European and American; the results of the former being positive, the latter negative.

Selter,[18] in Germany, sprayed his own throat and that of his assistant with a saline solution filtrate of throat washings of several patients, and both developed a mild attack of influenza. He emphasized especially the possible symbiotic relationship between the filtrable virus and the commonly present diplostreptococcus.

The French workers, Nicolle and Lebailly,[19] injected the unfiltered and filtered bronchial secretion in salt solution from an influenza patient 3 days ill into 2 monkeys under the conjunctiva and intranasally. They developed symptoms of the disease. Two volunteers were inoculated subcutaneously with the filtrate (bougie Chamberland L 2, pressure 30-40 cm. Hg.), and both came down with the disease. Intravenous inoculations in a man and in monkeys with bronchial filtrate and with unfiltered blood gave negative results.

The British investigators, Gibson and Connor,[20] state that they inoculated two rhesus monkeys subconjunctivally and intranasally with filtered human influenza sputum and obtained positive results, thereby confirming the work of Nicolle and Lebailly. They call especial attention to the hemorrhagic exudate in the lungs of one of the monkeys killed for examination. Influenza bacilli were not found.

[17] Jour. Am. Med. Assn., 1918, 71, p. 1733.
[18] Deut. med. Wchnschr., 1918, 44, p. 932.
[19] Presse méd., 1918, No. 58, p. 537.
[20] Brit. Med. Jour., 1918, 2, p. 645.

Opposed to these positive results are the far more extensive experiments, of a negative character however, reported from this country. Nuzum[21] inoculated the throats of several volunteers with nasopharyngeal washings from typical cases with negative results. Also two monkeys were inoculated with filtrate of the bronchial mucosa and filtered throat washings without results.

From the Public Health Service and the Navy[22] recently come the reports of extensive transmission experiments at Boston and San Francisco. At Boston 68 men were inoculated, some with Pfeiffer's bacilli and others with unfiltered and filtered secretions, all without results. At San Francisco 10 men inoculated with Pfeiffer's bacillus or its filtrate did not react. Forty other men inoculated in various ways with unfiltered and filtered respiratory secretions all yielded negative results. One is impressed with the large scale on which the American experiments were conducted; and one is tempted to criticize the European experiments because of the few subjects used and the possibility of natural infection. McCoy and Ritchie in the San Francisco experiments call attention to 3 cases of tonsillitis following the inoculation of unfiltered material caused by hemolytic streptococci. This would appear to be an experimental transmission of streptococcus sore throat. Might some such infection explain the apparent positive results of the European observers?

It is evident that these experiments cannot be considered conclusive one way or the other, and many more are clearly indicated. It is difficult to understand these negative results following inoculation with such material as unfiltered secretions. They are not at all in harmony with our ideas of the transmissibility of the disease under natural conditions.

In connection with these experiments with filtrable viruses it is interesting to recall the positive experiments of Kruse[23] in Europe, and Foster[24] in this country, in the transmission of common colds to human beings, using a filtrate from the secretions of infected persons. The filter passers of measles, scarlet fever, poliomyelitis, smallpox, vaccinia, foot and mouth disease, pleuropneumonia of cattle and fowl diphtheria, all involving more or less intimately the respiratory

[21] Jour. Am. Med. Assn., 1918, 71, p. 1562.
[22] Pub. Health Rep., 1919, 34, p. 33.
[23] München. med. Wchnschr., 1914, 61, p. 1547.
[24] Jour. Infect. Dis., 1917, 21, p. 451.

passages, naturally lead one to seriously consider a similar agent as the primary cause of influenza.

Whatever the primary agent may be, it would seem to be clear that the more serious aspects of the disease — the complications and death — are caused very largely by pneumococci, streptococci and influenza bacilli acting alone or often together. In this respect it closely resembles other respiratory diseases like scarlet fever and measles.

THE CLINICAL PICTURE OF THE INFLUENZAL EPIDEMIC OF RESPIRATORY DISEASE

Solomon Strouse

Feb. 21, 1919

No matter by what name the disease is called it was to all intents a new disease for most practicing physicians. To handle the pandemic we had to be in the attitude of mind which Henry Adams describes as the result of a Harvard College education in the 50's, "open, free from bias, ignorant of facts, but docile." Yet even after 5 months' steady experience, I hesitate in the attempt to paint a clinical picture of a disease which in December and January is so different from what was apparently the same disease in October and November.

It is necessary to consider the disease from the point of view of its various phases and to allow each phase its own place in the composite picture. The first phase was the highly virulent type of late September and early October which gradually waned through November. In December a second wave, much milder in intensity, appeared with a clinical picture different from that of the first wave. In January patches of color from both phases are seen on the canvas. The disease then is essentially an infectious and contagious disease of the whole respiratory system from nasal orifice to lung alveoli, with a special predisposition to the production of capillary bronchitis and lobular pneumonia. The incubation period usually is from 24-48 hours, occasionally longer. The onset is acute with prostration, fever without definite chill; cough or the symptoms of pharyngitis, rhinitis, and conjunctivitis. The course is uncertain, varying from 2-12 days or longer, depending almost entirely on the presence and extent of bronchial and pulmonary involvement. The complications are few, empyema, lung abscess and otitis media being the most common. The sequelae are multiple, and might be encountered in almost any part of the body. Post-febrile prostration may be considered the most constant after-effect.

This definition of the disease presupposes the impossibility of separating during the pandemic various types of respiratory disease which might not be influenza. The second wave (December) was comparatively mild and in many instances was limited to slight involvement of the nasal mucosa. In October the throat usually showed

slight injection of the anterior pharyngeal pillars; in January and February an edematous, very injected throat was common. Yet justification for the inclusion of all types is easily found in the many instances of multiple family infection. In December a wife nursing her husband, then a child with the mildest nasal infection, would after the proper incubation period herself become ill with the typical virulent form of the October wave. The importance of the conception of the pandemic in all its phases as a single disease will be emphasized later in the discussion of treatment.

Little need be said in detail concerning the clinical aspects of the mild type of case, except to point out what has already been mentioned by many writers, namely, the potential dangers of even the mildest case, which during the epidemic should be considered serious from the onset of the earliest symptom and should receive the same treatment as the apparently more severely ill patient. It will take many thousands of carefully examined cases to determine the percentage of incidence of lung involvement; since the difficulty of picking out consolidated areas is not easily met by even the best clinicians, and consequently reports will vary with the skill as well as with the interpretation of the observer.

But that pneumonia, lobular or lobar in type, is the most common serious accompaniment of the disease is recognized by all clinicians. Although this interpretation of the disease is not the same with all observers, I do not by any means consider pneumonia a complication; it is merely one form of the infection. An attempt to group the cases of pneumonia into various anatomic types seems untenable from the facts obtained by continuous observation of the same patient. It was no uncommon occurrence to find the 2-day fever followed by a day or two of apyrexia, then a return of fever with a small patch of râles somewhere in the lungs. This small patch of râles might easily, within a few days, extend until the chest was like a checkerboard; it might disappear entirely to be replaced by another patch elsewhere, or it might turn into a frank lobar pneumonia or even lung abscess. And altho the severity of the clinical picture was apt to run parallel with the extent of the pulmonary involvement, it was not at all unusual to have an acute hemorrhagic pulmonary edema end the life of the patient with only a few râles at a base.

If any grouping is possible, it must be accomplished from the whole clinical picture rather than from the extent of lung involvement.

The ratio of temperature, pulse and respiration, the general appearance of the patient, the grade of cyanosis, the character of the pulse, the degree of mental disturbance gave the only pointers of value in determining severity. At the beginning of the epidemic we unfortunately met the most virulent type of disease. Patients ill only 24-48 hours were overwhelmed by a toxemia, the intensity of which was appalling; and all such patients died. Yet perhaps the most striking element of the whole first wave was its uncertainty. Perhaps a majority of the serious pneumonias we saw followed a period of apyrexia, although of course many had small pulmonary or bronchial patches from the beginning.

The individual symptoms and signs have become so well known that it is only necessary to mention them in passing. The temperature varied from 99 or 99.5 to 105 F., and seemed to bear no constant relation either to the pulmonary involvement or the severity of the illness. Some of the patients who later became severely ill were afebrile at onset. The pulse usually was slow; a rate of 100 or less with a temperature of 104 was not uncommon. Leukopenia — 2,000 to 6,000 was the rule; a count higher than 10,000 caused a search for empyema or lung abscess, except in a few instances of uncomplicated pneumonia. The respiratory rate also often gave no index of the extent of pulmonary involvement; although an ascending pulse and respiratory curve indicated increasing toxemia. Pleuritic pains were not frequently complained of. A hard harassing cough in many instances produced severe muscular pain in the abdomen. The sputum usually was thick and mucopurulent; later tinged with bright blood, or even purely hemorrhagic. The characteristic color changes of pneumonic sputum were interesting by their rarity. The blood pressure usually was low, and as Bloch has pointed out, this was particularly noticeable in the diastolic pressure. Urinary changes except for febrile albuminuria were negligible, although mention must be made of the early persistent anuria, especially of women patients. Premature menstruation was common on the 2nd to 4th day of the disease. Gastro-intestinal disturbances or the so-called gastro-intestinal influenza were exceedingly rare in our experience.

The progress of an individual case was always full of exciting adventures into no-man's land. Cardiac dilatation, always the scarecrow to frighten us in regular pneumonias, appeared in this disease rarely, except at the end of an extreme toxemia. Yet cyanosis of the

most striking hues was met with. In some instances the lips actually looked as if they had been touched up with blue paint; in others the mucous membranes were red, but the skin had the waxy cyanosis of death. Whatever the immediate cause of this cyanosis may be, it certainly was of grave prognostic significance.

Some of the patients looked as if they were suffering from acidosis, yet as far as I know acidosis has not been shown to occur; others gave the distinct impression of respiratory failure; and in many instances acute hemorrhagic edema would appear like the ghost at the feast when all seemed well. It would seem as if the only possible physiologic explanation of the cause of death in some cases could be found in a toxic paralysis of vital functions of the central nervous system.

Almost everything known in pulmonary pathology could be found and the changes in a single patient from day to day were at times as wierd as they were confusing. We learned early in the epidemic (but not early enough) that the persistence of fever after the 3rd or 4th day usually meant pulmonary involvement; yet in some cases repeated examinations by several men would fail to reveal any pulmonary signs. In some cases, however, a continued fever could be accounted for by complications such as pulmonary tuberculosis; in others nothing was found to explain the fever as, for example, the nurse whose temperature ranged around 105 F. for 2 weeks, but whose lungs were persistently negative to physical examination and the roentgen ray. In many cases râles could be heard at one base in the morning, to disappear at night time and be replaced the next morning by the signs of lobar consolidation in the other lung. Typical combinations of the physical signs of consolidation were indeed rare; slight dulness, or some prolongation of the expiratory note might be found; but in many cases, except of frank lobar pneumonias, we had to be content with râles. We saw many patients with one unquestioned spot of pneumonia, but with the rest of the lungs diffusely spotted with râles. This condition might be called the "wet lung."

Mention has already been made of the acute hemorrhagic edema, but the phenomenon is so new as to warrant further discussion. Many times patients, who were doing exceedingly well in every respect, whose temperature was declining or normal, would suddenly be struck by something causing tremendous distress, violent coughing and choking, with the expectoration of a bloody frothy fluid. The lungs

were filled with fluid and the patient died within a few hours. This was not associated with cardiac weakness, and as far as I know still remains unexplained.

The development of empyema or pulmonary abscess could be forecast by a leukocytosis and persistence of fever, rather than by characteristic changes in the physical signs. In fact, signs of fluid were so common that at one period we did exploratory thoracenteses on a large number of cases in which doubtful signs were present, and usually obtained a clear or sero-sanguineous fluid. Both empyema and abscess occurred later in the course of the case. The roentgen ray was the most successful single diagnostic aid. During the period of the later wave uncomplicated, delayed resolution was much more common than in the early wave. This can probably be explained by increased resistance in the later cases. Patients with pneumonia died in the early wave before resolution began. In Chicago otitis media occurred fairly frequently as a late complication of the October wave, but in nothing like the proportions described for the pandemic of 1889-91. Perhaps the one bit of sunshine in the whole epidemic was found in the possibility of recovery — functional and anatomic — which can be demonstrated by repeated roentgen-ray examinations of some of the chests literally riddled with various pathologic changes. Some examples of these changes are here shown.

Complicated by other diseases, influenza seemed in no way more severe than in the uncomplicated cases. Patients with even decompensated valvular heart lesions passed through the infection with no more or less trouble than normal persons. Patients with chronic nephritis, Hodgkin's disease, bronchial asthma, Graves' disease, survived in the same proportion as normal individuals. The complication with pulmonary tuberculosis even seemed to be no more severe; although two of my patients had an acute flare-up of their tuberculosis after the influenza. It will be interesting to note whether the infection will have any after-effect on the progress of the chronic fibroid tuberculous patient.

The generalization concerning the harmlessness of serious complicating diseases does not include the terrific effect of the disease on what we usually consider a normal physiologic state: in pregnancy. In October the combination of influenza and pregnancy furnished a death rate, according to many statistics, around 60%. In December,

fortunately, pregnant women were included in the general fall in mortality.

Both the incidence of the disease and its mortality are tremendous. At the Michael Reese Hospital were treated from Oct. 1, 1918, to Jan. 31, 1919, 655 cases of influenza and pneumonia. This number includes all cases from the moribund patients dying within 24 hours to the hospital personnel who were put to bed on the slightest suspicion of a respiratory infection. The hospital mortality figures give perhaps the worst possible picture of the disease. A large percentage of the hospital cases were moribund on entrance, or at least were at the end of a neglected period. The hospital personnel itself represents mainly doctors and nurses continuously exposed to the disease in its worst form. Of the total, 108, or 16.5% died; but the rate would be about 13% if the patients dying within 24 hours were excluded. The accompanying table illustrates very well how the deaths were grouped; and figures given in percentage of deaths to total infections in any specific group show variations from 4.5% in the female personnel (mainly nurses) to 25% deaths in the male adult group. Of a hospital personnel of approximately 400, there were 147 infections with 9 deaths, 6.1%, which was, excepting female personnel, the lowest death rate of any group.

TABLE 1

INFLUENZA-PNEUMONIA MORTALITY

655 CASES

Average		16.5%
Male adults		25.
Total adults		22.
Female adults Male personnel Total males		20.
Total females		14.4
Children	Female	13.4
	Total	13.
	Male	12.6
Total personnel		6.1
Female personnel		4.5

It is worth calling attention to certain facts which bear on the extreme contagiousness of the disease. We lost 4 nurses and 3 interns. There were 108 nurses who, from late September to Jan. 31, 1919, had respiratory infections which, according to the definition given in the early part of this paper, belong to the disease under discussion; and of these, 43, or practically 40%, were working in the influenza wards at the time of their infection. Yet the number of nurses working in such wards at any time never exceeded more than 20% of

Case 1.—Oct. 22, 1918. Shows extensive pulmonary involvement.

Feb. 21, 1919. Shows almost complete clearing up of the lung.

Case 2.—Dec. 11, 1918. Pulmonary abscesses.

Dec. 19, 1918. Shows disappearance of the abscesses with some scar formation.

Case 3.—Oct. 25, 1918. Diffuse pulmonary changes.

Feb. 17, 1919. Practically complete healing.

the total nursing force of 150. The pneumonia incidence among the nurses cannot be given in figures, simply because the rush of work prevented good records. Yet I know definitely of 20 cases, of which 12 (60%) were among nurses working in the influenza wards. And the 4 nurses and 3 interns who died *all* had been on duty in these wards.

The bacteriologic work done by Drs. Howell and Brown showed that the air in the influenza department contained a streptococcus indistinguishable from the one they were regularly recovering from blood cultures on patients.

In private practice the mortality figures apparently were not nearly as distressing as those just quoted. It was simply impossible to keep accurate records of one's private work during the course of the epidemic, yet the impression is definite that the death rate, even among those patients who developed pneumonia, was considerably lower than among those seen in the hospital wards.

From the discussion so far given it is clear that it is impossible to forecast a prognosis. The danger of death lurked in every case, no matter how mild the onset, how short the initial fever, how few the râles. And after this fact was driven home the question of treatment became simplified. It would be a waste of time to recount the early days of the epidemic, when day and night we struggled to discover the relative therapeutic value of atropin, morphin, digitalis, or what not. Suffice to say we have tried practically everything; one week using the salicylates, the next discarding them because we thought them depressing. Hexamethylenamin, alcohol, intravenous injection of large doses of quinin, digitalis, caffein, camphor, pituitrin, epinephrin, oxygen, creosote have been tested out; and at present we do not hesitate to say that no medical treatment is advised except to relieve symptoms; acetyl-salicylic acid or an opium alkaloid for pain or cough, and digitalis in the more severe cases to support a weakening heart are the only drugs needed. Atropin perhaps is of avail in checking some cases of "wet lung."

But though we are pessimistic of the value of drugs, we believe there is a definite therapeutic plan of attack, which, to be successful, must be rigidly carried out. The comparatively low mortality of hospital personnel and private patients must be due in part to definite ability to place these patients in bed and keep them there. Referring back again to the definition of the disease as a general infection of

the respiratory tract, every patient who during the pandemic suffers from respiratory infection, is potentially an influenza pneumonia, and must be treated as such before the pneumonia develops. Every such patient should immediately take to his bed, keep warm in a well ventilated room, individual prophylaxis instituted, and the bed-pan habit insisted on. Then plenty of water and as much substantial food as the patient will take are given; the bowels kept open by mild cathartics and the patient kept in bed 48-72 hours after the temperature becomes normal. External hydrotherapy has been of exceedingly doubtful value. It is, of course, true that many persons are unnecessarily put to some hardship by such a plan which in not all instances is practical; yet we cannot help feeling that the lives of some are saved. As Dr. Hamburger has stated in discussion, the charts of Colonel Vaughn clearly indicated a definite relationship between mortality figures and early taking to bed; and in the face of a combination of these figures and the inability to make specific diagnoses during the epidemic, it is clear that the therapeutic plan just outlined is essential.

Discussion of the use and value of vaccines and serums in the therapeutics of the disease must be left to those with a more extensive experience. Our own cases are comparatively few, and though they give an impression of wasted endeavor, we hardly feel competent to express an opinion.

A word about reinfection: This may be considered under two headings; (1) reinfection during the course of the illness, and (2) late infection of a patient who had been previously sick with the disease. Regarding the first point, little of definite value can be stated. The wide range of bacteriologic findings makes it possible to conceive of a patient ill perhaps with a mild infection from the influenza bacillus becoming secondarily infected with the streptococcus. The clinical picture of many cases suggests this possibility, and the recent report from one of the camps seems to verify this supposition. Certainly the apparent recrudescences in patients who were getting along well warrants serious consideration of a problem of individual prophylaxis as a means of combating secondary infections.

Regarding the point of actual secondary infection in a patient previously sick, this question is naturally a bit difficult to settle. It is true that some patients with a mild respiratory infection in October became victims of pneumonia in November, or vice versa; but the

inability to make a specific diagnosis may account for some apparent reinfections of this type.

The after-effects of the disease have been many and varied. The depth of physical distress following even a 3 days' illness could not be believed, except by one "who too has suffered." In some cases the extreme physical fatigue was unquestionably due to weakened heart muscle; yet endocarditis and pericarditis have been scarcely noted. Pulmonary embolism and femoral thrombosis have occurred, usually about 7 days after a normal temperature. I know of two cases of each. Psychoses in our experience have been rare; one patient developed a low grade, toxin infection psychosis during the fever; one patient who had influenza, several weeks later developed dementia præcox. The history of the latter case suggested an unstable nervous mechanism before the attack of influenza. Loss of hair and mild menstrual disturbances have been common. Persistence of cough, often without any discoverable chest lesions, has occurred so frequently as to be taken for granted. Pains around the chest are frequently complained of for weeks, but pleurisy has been very rare. Permanent renal damage has not been noted. Signs of hyperthyroidism have been noted in several patients, but whether they were present before the onset of the infection we do not know. "Encephalitis lethargica" is now being found occasionally.

THE PATHOLOGIC ANATOMY OF INFLUENZAL BRONCHOPNEUMONIA *

E. R. LeCount

Feb. 21, 1919

In this report, based on approximately 200 necropsies, no attempt will be made to distinguish between changes due to the unknown virus and those from mixed or secondary infection; only the most outstanding features are discussed.

Perhaps the most lasting impression from long association with lobar pneumonia in postmortem examination is that when it alone is responsible for death, with very few exceptions,[1] a considerable part of the total pulmonary parenchyma is consolidated, undistensible and heavier than normal; even when limited to one upper lobe, that lobe is as a rule huge, and the lung weight as a consequence frequently doubled.

Therefore, the first feature of the lungs in influenza to attract attention was the relatively small amount of lung tissue solid with grossly demonstrable pneumonia. Even when measured, the total of such regions is so small that it is difficult to ascribe death to the pneumonia with an assurance at all comparable to that with which death is accounted for by lobar pneumonia; in fact, the amount of lung tissue in influenza actually pneumonic seems too little in many cases to explain death by pneumonia. This is best shown by distending the lungs with air, for many of the dark red or purple places, apparently airless and semisolid, balloon out and become quite pink. When surfaces are made by cutting tissues actually pneumonic from influenza, it is not common to find gray or gray-red and finely granular plugs of fibrin and cellular exudate which come away on the knife, as is the case in lobar pneumonia and most bronchopneumonias other than those of the influenzal type. Such surfaces in the nondistensible places in influenzal pneumonia are wet, "velvety" and not granular, but smooth; they resemble raw meat or wet skeletal muscle. The redness of the button-like, firm, superficial regions of pneumonia, likened by some observers[2] to hemorrhagic infarcts, is due perhaps as much

* From the Pathological Laboratory, Rush Medical College. Influenza Investigations, U. S. Public Health Service.

[1] Compare report by Clark and Batman (Jour. Infect. Dis., 1904, 1, p. 229) on capillary bronchiolitis, with the symptoms of lobar pneumonia including a crisis.

[2] Abstracts of Foreign Literature Compiled by the British Medical Research Committee, Jour. Am. Med. Assn., 1918, 71, p. 1575.

* From the Pathological Laboratory, Rush Medical College.

to the well-preserved cells of the exudate, many of which are mononuclear, as to the blood content.

However, ranking in importance with the relatively small amount of actually pneumonic lung, or perhaps entitled to first place as a conspicuous feature, is the huge, often thin and watery bloody exudate in the lung tissue and bronchioles. This bloody fluid, on the development of rigor mortis, often pours out of the nostrils so as to stain a large part of the white sheets in which bodies are wrapped. It mainly is responsible for the low level to which the lungs sink when put into water and for the total submersion of some; many are like the lungs of the drowned. The fluid mixed with air and forming a blood-tinged froth is abundant in the trachea, larynx and large air passages after death. Accumulating under the visceral pleura, it makes one of the most interesting and tell-tale signs of influenza; for normally the pleura, fitting the underlying lung tissue snugly as a transparent membrane, allows every detail of the coal-dust mosaic-like markings, as well as the coarser details of the pink, air-containing vesicles, to be clearly seen; but, with the presence of this bloody fluid in the subpleural lymph vessels in abundance so as to distend them, there are produced opaque, reddish brown places, usually a few centimeters in diameter, frequently seen at once when the sternum and costal cartilages are removed. They are so distinctive that influenza is at once suggested as the cause for death; and when no clinical details are known, are highly important clues as to the cause of death. This dissection of the outermost layers of the pleura is very common in the angles formed by fissural surfaces — in the bottom of the cleft. Small hemorrhages in the pleura are also common.

Another feature also due to this bloody exudate is that usually there is some fluid of the kind just described in one or both pleural cavities—more, as a rule, on the side of greater lung involvement. Now, with most pneumonias the pleural exudates are not so blood tinged. With lobar pneumonia they are not only commonly yellowish but also heavy with fibrin; large masses of yellow fibrin wet with plasma often make the lung in lobar pneumonia actually "shaggy"; this I have not seen in influenza. There is commonly some fibrin on the lung, but search is often necessary to find it. It is seldom more than 1 mm. thick, and is often less. The amount of the blood-tinged fluid in the pleural cavities varies widely. When measured, from 25-100 c c are frequent; larger amounts have been weighed, and the

following weights will serve as examples of these exceptional instances: fluid in the right pleural cavity, 840, 345, 860, 600, 320, 930 and 600 gm., each one case; fluid in the left pleural cavity, 900, 1,000 and 320 gm., each one case; 660 gm. in the right with 800 gm. in the left; 1,120 gm. in the right with 1,140 gm. in the left, each one case. These large collections of fluid are in no sense "empyemas." The fluid is only slightly turbid. When time has elapsed for sedimentation after death, the fluid taken for bacteriologic examination, if the pipets are not introduced too deeply, is quite transparent and clear, often with a little of the lilac tint of hemolysis; that collected from deeper layers is turbid.

This bloody exudate is not pus in the sense that pus is the product of liquefaction necrosis; there is no suppuration. Postinfluenzal empyema, however, does occur, as well as empyema with repeated thoracentesis. This thin, characteristic, bloody exudate of influenza contains only a little fibrin; or none at all may be visible grossly. It is unlike the pleural exudate of any other form of acute pneumonia with which I am familiar. It reminds one most of the inflammatory exudates in such places as the arm from acute sepsis following wound infection, or the thin, bloody fluid of woody phlegmon of the neck; it is more like exudates due to streptococcus than those we are familiar with in pneumococcus inflammations. The fat of the thymic body and other mediastinal fat, as well as all of the tracheobronchial lymph glands, are also often thoroughly wet with this fluid.

Since so much fluid was found in the lungs and as part of an exudate which in many instances escaped into the pleural cavity, less because of pleuritis there than because the lungs, so to speak, "overflowed," the lung weights were compared with the weights of lungs in lobar pneumonia. This comparison is shown by the accompanying charts of the ratio of lung to body weight.[3] From the charts it is apparent that the ratio of lung weight to body weight in lobar pneumonia and influenza are roughly similar; whereas with lobar pneumonia, the precipitate of fibrin is considerable, other parts of the pulmonary parenchyma being compensatorily emphysematous, in influenza, the pneumonia is less and the increased weight due in large part to fluid.

[3] The normal line is the 1.5 per cent. of the body weight, or 1: 66, as given by Vierordt (Anatomische, physiologische und physikalische Daten und Tabellen, Ed. 3, 1906, p. 44).

The pneumonia of influenza is commonly referred to as bronchopneumonia. It may be so designated, but it differs from other bronchopneumonias in its predilection for the periphery of the lungs and in the extent to which the inflammation is hemorrhagic.[4] These features, as well as the relatively little consolidation, are well shown by the following account, which may be taken as fairly typical of conditions found with death early in the disease:

> The upper lobe of the right lung is easily ballooned out with air, likewise the middle lobe, so that the black places due to coal dust are very black, the intervening lung tissue pale gray or pink. Except for a place 4 by 2 cm. on the mesial surface of the upper lobe where fibrous adhesions were torn, the pleura is smooth. There are two solid places in the back of the upper lobe, and the pleura covering them is a little swollen. These are 3 by 4 by 5 cm., not at all sharply outlined, with moist gray plugs (hand lens) in the air sacs which cut so as to leave smooth wet surfaces; a thin, watery red fluid comes out of the minute bronchioles in them. The lung tissue around them is very wet, but contains air; their bronchi contain a thin fluid with opaque flocculent masses in it. Another similar solid place near the front margin of this upper lobe, 5 to 6 cm. in diameter and 1 cm. from the pleura, has a good deal of blood in it. A solid place is in the back of the lower lobe, like the others but with a layer of fibrin on the pleura over it, as thin as transparent paper. This is also very superficial, and the bronchus to it is full of a frothy, thin, red fluid. A fifth place, from 5 to 6 cm. in diameter less sharply outlined, with thin fibrin on its pleura and 2 cm. deep (the third dimension), is in the lower lobe near the diaphragmatic surface, which is about one-third covered by fibrin. All the bronchi to this lobe contain these flocculent masses, some adherent to the lining. In the depths of this lobe about the large bronchi there is some consolidation 1 to 2 cm. wide, sharply outlined and deep red. Except in these solid places this lobe distends easily with air, as does the middle lobe, which has no solid places.
>
> The pleura of the left lung is smooth, and both lobes distend completely with air except in two solid places 2 to 4 cm. in diameter, one in the front of the upper lobe and 1 cm. deep, dark red and apparently full of blood, the other in the lower lobe and in all essentials similar. The first of these has sharp margins at lobule septums, and the pleura covering it is raised and translucent. In the smaller bronchioles of the left lung there is a little creamy mucopus.

There was a little slightly turbid bloody fluid in each pleural cavity.

Next in importance as a characteristic of this disseminated pneumonia, hemorrhagic in its early stages and phlegmonous later, is the change in the medium-sized and smaller bronchioles to the involved lung tissue. Early their linings are simply red, their channels filled with a thin, blood-stained froth or fluid; later the linings are necrotic and their content either a thin mucopus resembling that of early

[4] Symmers, in consequence of the hemorrhages, has compared influenzal pneumonia to that of pneumonic plague, Jour. Am. Med. Assn., 1918, 71, p. 1482.

gonorrhea or such a mucopus with small flocculent gray or gray-brown masses in it; slight dilatation of the smaller bronchi is common.

The brain substance is quite regularly swollen, the convolutions of the cerebrum flat; and although this may be evident at once by examining the head first, it is also very well shown by comparing segments made by coronal sections of influenzal brains after hardening

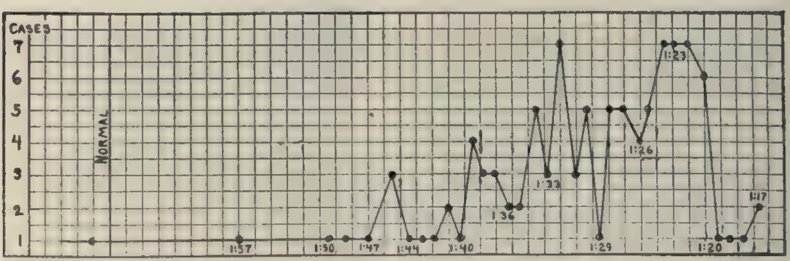


Chart 1.—Ratios of lung weight to body weight in 103 cases of lobar pneumonia from necropsies in 1915 and 1916.

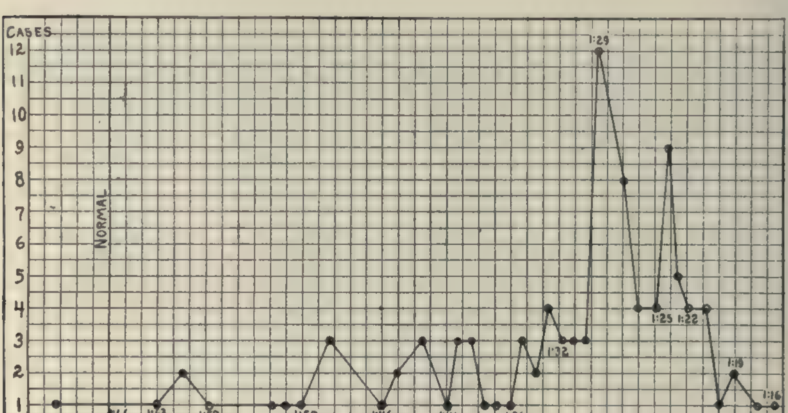


Chart 2.—Ratios of lung weight to body weight in 100 cases of influenzal pneumonia.

in formaldehyd with other brains similarly treated; they are not so swollen as are the brains of septic abortion or other forms of generalized streptococcus infection, nor so pale; but the even external contour and narrowness of the lateral ventricles is a conspicuous feature of influenza; this edema of the brain substance is less than that of uremia or heat stroke.[5]

[5] McKenzie, Pierce, and LeCount, E. R.: Jour. Am. Med. Assn., 1918, 71, p. 260.

Still another feature of influenza is that the spleen is not so large as in lobar pneumonia. This statement is a general one and is made without reference to the stage of either disease. The kidneys are regularly the seat of cloudy swelling, and have tense capsules. If any gross alteration of the liver deserves mention as fairly constant, it is the presence of patches of yellow on the front surface due to superficial fatty change.

Less constant are generalized icterus; the early appearance of staining of the lining of large blood vessels by laked blood; patches of necrosis of the larynx or trachea lining; hyperplasia of the lymphoid tissues of the thorax and neck; slight acute serofibrinous pericarditis; acute interstitial emphysema of the lungs and mediastinal tissues, or of these with subcutaneous tissues as well; otitis or accessory (nasal) sinus inflammation, or actual suppuration as small abscesses in the lungs.

It is difficult to believe that a disease with so many distinctive features and affording, as it has, so much of novelty in pathologic anatomy can fail to possess a correspondingly definite etiology.

A more complete report with results of microscopic studies will be made later.

PUBLIC HEALTH MEASURES AGAINST INFLUENZA

Heman Spalding
CHICAGO
Feb. 21, 1919

Influenza is a disease conveyed from person to person by close contact with a person having the disease, or a carrier of influenza infection.

The infection is conveyed through the air by coughing, sneezing, spitting and forceful talking. It probably is air borne on dust blown about by the wind.

The infection is conveyed by contact in kissing, on the common drinking cups and towels, and on hands and handkerchiefs soiled with the discharges from the mouth, nose and eyes. The disease travels no faster than the modes of travel of man permit.

The places where the disease is most frequently conveyed are, of course, where adults are most thickly crowded; department stores, elevated trains, suburban trains, street cars and passenger elevators in large office buildings.

In a less degree, theaters, moving picture shows, churches and other public assemblies are places where infection is disseminated. Dance halls, while not crowded, are dangerous because dancing is a violent exercise in a warm room, and deprives those who frequent such places of much sleep. Going from a dance hall tired, sleepy and in a perspiration adds to the danger of contracting influenza.

To combat an epidemic of influenza in a large city where the great industries require the congregation of large numbers of persons in confined places is entirely a different problem from that presented in small cities and towns. To stop all the great industries and means of travel in a large city would paralyze business, throw out of employment thousands who would suffer for the want of the necessities of life. Such a course would cause more sickness and death from cold, hunger and want than would be prevented or saved by shutting down these activities. In the face of an epidemic, we must do many things that can be omitted when epidemic conditions subside.

At the present time in Chicago, we isolate or hospitalize the patient until well, and in case of school children and teachers who are contacts in the family, they are excluded from school for eight days.

An individual sick with the disease that is conveyed from person to person by close contact should be hospitalized or quarantined at home, but when an epidemic comes on a city in the manner of an avalanche, quarantine in the usual way, or hospitalization of the hundreds of thousands of the afflicted is practically impossible. Under such conditions, the best we can do is to hospitalize to the limit of the capacity of the existing hospitals, and for the rest, secure isolation and restriction of contacts through cooperation with the physicians and families afflicted.

To meet epidemic conditions of influenza, I would suggest the following essentials:

1. All cases should be reported to the Commissioner of Health.
2. Hospitalize or isolate all cases.
3. Allow no visitors in hospitals receiving influenza.

The public and doctors should be instructed what to do to avoid contracting the disease and how to prevent conveying the infection to others, through bulletins, circulars of information, the newspapers — daily and weekly — in various languages, placards in the street cars and other public places, public addresses and talks in churches, theaters, moving picture houses and schools. Information should be conveyed to the public through every channel of publicity available. A useful placard for display in street cars and public places is the following:

> SNEEZING, COUGHING, SPITTING IN PUBLIC PLACES HELP TO SPREAD SUCH DANGEROUS DISEASES AS INFLUENZA, PNEUMONIA, DIPHTHERIA AND CONSUMPTION. IN 1917 THE GERMS THAT CAUSE THESE FOUR DISEASES KILLED 10,220 PEOPLE IN CHICAGO. COVER YOUR MOUTH AND NOSE WHEN YOU SNEEZE OR COUGH AND HELP TO KEEP CHICAGO HEALTHY.

People will make good use of knowledge if it comes to them from a source in which they have confidence. In the face of danger, even the indifferent will listen to the words of the health officer.

Explain to the public the benefits and disadvantages of wearing a mask. They should be told frankly what is known about vaccine as a prophylactic in influenza. I would not close schools if there is a school inspection service. School children are less susceptible to the disease than those in the period from 20-40. From 5-20, about 5% of deaths from all causes are caused by acute respiratory disease or influenza, while in the age period from 20-40, over 21% of deaths

from all causes go to influenza or acute respiratory diseases. The school is a good place to give out information and to learn of the presence of influenza in the homes of the children. Suspect children can be isolated in a room when they come to school, a mask temporarily placed on their mouth and nose until the doctor examines them. Those not free from symptoms of influenza are sent home. The schoolrooms should be superheated in cold weather and the windows open for suitable air. If the school is closed, the children are running about with no one to look after them, while in school they are under the care of a doctor, a nurse and teachers for several hours each day. I would not close churches or necessary public assemblies. I would not close department stores, nor stop street cars running. The policy followed in Chicago which brought gratifying results was to allow essential business to continue and prohibit unnecessary public assemblies. Under this policy, theaters of all kinds were closed, cabarets, dance halls, athletic meets, lodge halls, skating rinks and everything in the amusement line.

This was a benefit in several ways. It allowed persons to get more sleep and remain at home. Closing of night entertainments forced home-staying, as there was no place to go. The places were aired and cleaned. The proprietors suddenly awoke to the necessity of making their houses safe places for the public. This was a sound policy. My plan would be to close these unnecessary assemblies temporarily only, say, for an evening or two. Then open them up under supervision and use them as places from which to give out information on how to prevent the spread of infection. The closing would be for educational purposes. The importance and gravity of the epidemic would in this way be quickly impressed on the minds of an enormous number of citizens. The effect is decisive and when followed by instruction is more or less permanent.

I believe a few lines of instruction thrown on the screen in the moving picture shows are of the greatest educational value. The following flashed on the screen will serve a good purpose:

> DO NOT DO ANYTHING TO OTHERS YOU WOULD NOT HAVE THEM DO TO YOU. THEREFORE, IF YOU HAVE A COUGH OR COLD, OR SYMPTOMS OF INFLUENZA, GO HOME AND STAY THERE UNTIL FREE FROM THESE CONDITIONS. IF YOU MUST COUGH OR SNEEZE, PLEASE HOLD YOUR HANDKERCHIEF OVER YOUR NOSE AND MOUTH. KEEP YOUR HANDKERCHIEF WHERE YOU CAN REACH IT BEFORE YOU COUGH OR SNEEZE.

The mask properly worn and changed several times daily no doubt helps protect against influenza, but as it is worn by most people, it is worse than useless. A doctor or nurse in the presence of a patient can wear the mask and should do so, for they can wear it intelligently, but the general public will not and cannot be intrusted to use it properly.

The cities where the mask was worn showed no better death rate than those where it was not used. Chicago used it only incidentally, and our excess death rate was 2½ times less than that of San Francisco, where the mask was worn.

It can be used temporarily on school children who are suspected of having the disease, while waiting for the arrival of the school doctor.

The proof that vaccine prevents influenza is meager. Its use in Chicago no doubt helped to keep the people from becoming panicky, but we must have further proof before accepting it as a prophylactic. Inasmuch as its use is practically harmless, there can be no objection to its administration.

The method pursued in Chicago gave results, as Chicago escaped with the lowest excess death rate of all the large cities except Cleveland. According to the U. S. Census Bureau, Chicago's excess death rate over normal is 2.2; Cleveland, 2.1; New York, 3.6, and Philadelphia, 7.1.

The health officer should point the way and secure the cooperation of every organized agency, private, municipal, state and national that is within his reach. He will need their help, for no health department is properly equipped to meet extraordinary epidemics. The best organized and equipped health departments in the country made the best showing in our recent epidemic — Chicago and New York.

DISCUSSION

DR. W. W. HAMBURGER: While the setting of definite dates for the beginning and end of an epidemic is somewhat an arbitrary procedure, the influenza epidemic at Camp Zachary Taylor may be said to have covered a 5-week period, starting Sept. 22 and ending Oct. 25, 1918. From the latter date on, sporadic cases continued to come in, so that on Dec. 17, 1918, there had been admitted to the base hospital, 12,742 cases with 822 deaths, a mortality of 6.45%.

During the period of the epidemic, there were approximately 72,000 troops in camp; 60,000 from Camp Zachary Taylor, 10,000 from the Firing Range at

West Point, and 2,000 from the Jeffersonville Quartermaster Depot, so that the gross mortality in the entire camp command was 1.14%.

The handling and study of the epidemic was alloted to four teams as follows: an epidemiologic, a pathologic, a clinical and a bacteriologic team; this plan of group study having been arranged by the chiefs of service. By this means, we were able to assign certain men to certain definite lines of investigation, and at the same time to obtain mutual cooperation and comparable results from the several teams. The members of the teams met with the chiefs of service in a daily conference and at the end of each week a Sunday morning conference was held, at which time informal reports from the several teams were presented. At these conferences the daily and weekly changes in the situation were discussed and compared.

The official report of the observation is still to appear, so that at present only certain general impressions and conclusions are available. These are summarized in the form of curves, graphs, charts, etc. Many of the curves were plotted daily during the course of the epidemic, so that by reference to them at the end of any 24-hour period we were able to follow such vital matters as the daily number of admissions, deaths, new cases of pneumonia, etc. These facts were of paramount practical interest and an aid in planning 24 hours ahead for such matters as bed capacity, opening up of new wards, and barracks, hospital nursing, and medical supplies of all kinds; also our daily reports to the public and the press and our predictions as to the number of deaths and decline of the epidemic, were based on these curves. As the study continued, week by week, the changes in the clinical and pathologic pictures as the epidemic waxed and waned were most absorbing.

We had at one time a 9,000 bed hospital. We had from 500 to 1,000 new cases every day. We had about 250 cases of pneumonia developing a day. Our highest death rate was 80 in 24 hours. We had from 150-200 medical officers and from 300 to 500 nurses. We had a pneumonia ward of 2,000 beds. We had a ward of from 3,000-4,000 beds for new cases of influenza, and a ward of from 1,500-2,000 beds for convalescent patients. These three hospitals were under the direction of the chief military head of the hospital. We had to plan 24 hours ahead so as to arrange for new beds.

The height of the epidemic was reached 9 days after its beginning. Then there was a drop, a pseudocrisis, a secondary rise, and then a permanent drop. The pneumonia curve is interesting. In the early cases the patients died on an average in 3 days after admission. Toward the height of the epidemic the duration of the pneumonia was increased from 3-4 days, showing a prolongation of the pneumonia period, as the result, perhaps, of the patients making a better attempt to fight the disease. The chronological chart of necropsies shows the change in the general pathologic picture from week to week. There was a change in the involvement of the liver, as shown in the increase of hemorrhagic hepatitis. There was a change in the suprarenals, first hemorrhage, and in the second stage congestion. The proportion of lobular pneumonia, that is, the hemorrhagic type, was very great in the first week. This was followed later by an empyemic picture with less hemorrhage. Changes were found in the terminal ileum and transverse colon, particularly in the first week in cases with blood in the stools. In the skin we found quite regularly a condition like the one in the ileum, a vesicular eruption. Cultures showed staphylococcus.

Three general conclusions were arrived at from our study of this disease:

1. Influenza is a disease of the entire body, involving the head and head sinuses, brain and meninges rather regularly. It involves the entire pul-

monary tract, as shown by hemorrhagic bronchitis and pneumonia. It involves the abdomen, as shown by the cloudy swelling of the liver, kidney and spleen, and by the clinical picture of hemorrhage, and the condition of ileum and colon. It involves the skin, as shown by the vesicular eruption. The pneumonia that develops is the most important thing. From our observations influenza is a generalized process, particularly striking, with an involvement rather constantly of all the sinuses of the head.

2. Influenza, as we saw it, was a progressive disease. The picture of the first week was quite different from that of the second and third weeks. In the first week the tendency to hemorrhage was striking, there being hemorrhagic sputum and hemorrhage from the lungs and the bowels. As immunity was established, this hemorrhagic tendency became less. Our conclusion from this was that the very early infection was most virulent and the efforts of the tissues to withstand the disease was evidenced by the hyperemia. In the first week the patients died within 24 hours, showing a generalized hyperemia. In the second and third weeks this condition changed to a consolidation in the lung.

3. The early cases showed rather generally the influenza bacillus. In the second and third weeks the Pfeiffer bacillus in the sputum was overtaken by the pneumococcus. Recent laboratory tests in new cases disclose an increased number of influenza organisms in the sputum and postmortem cultures. The necropsies in 5 cases made early in the epidemic showed Pfeiffer's bacillus with no other organisms, while 10 cases in the fourth week showed pure pneumococcus with no influenza bacilli.

DR. ROBERT B. PREBLE: It might be of interest to say something about the experiences which the army abroad had with the influenza epidemic. This epidemic began in the spring of 1918, was moderately severe, and then disappeared. Along the middle of September we began to have cases of pneumonia, and we found the hemolytic streptococcus both in the sputum and at necropsy. In the course of a very short period we began to find influenza bacilli, and these increased without our being able to detect any difference in the clinical manifestations of the disease or in the pathologic findings. Then the influenza bacillus began to disappear, and the whole thing was over. We had far fewer cases than you had here, and the cases were obviously milder in type. For example, in a camp of 25,000 men we had only 500 cases of pneumonia, with a mortality which ranged as high as 33%. As the streptococcus influenza went down and the pneumococcus became more common, the mortality fell to 10%.

Another curious observation we made was that influenza developing among surgical patients was unaccompanied by mortality. None developed pneumonia. This was curious because most of these patients had septic wounds, and we had a great many septic compound fractures; yet none of these patients developed pneumonia, and we had no mortality.

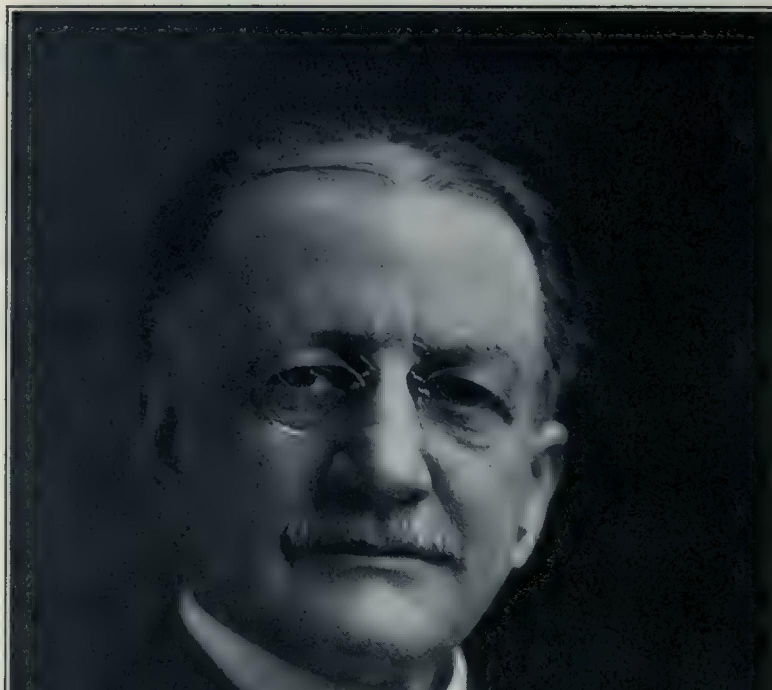
DR. JULIUS H. HESS: I want to report an interesting little group of cases at Fort Benjamin Harrison. In a measles and streptococcus pneumonia epidemic previously many of us had the idea that there was some association between the high mortality and typhoid vaccination. In the second week of the influenza epidemic 13 fresh recruits from North Dakota came into camp. They had not had triple typhoid vaccination. In that number the mortality was exactly the same as in all the other cases at camp that had had typhoid vaccination.

Of the symptoms there was one that stood out so prominently that I think it ought to be included as a prominent early symptom: the gangrenous odor on the breath of the patients. When one went into a ward that was not ventilated properly, the odor was just the same as one gets on coming into contact with an abscess of the lung. This odor was present in the first 48 hours, so it could not be associated with later complications.

We found that more than 70% of the throat smears and sputums showed a large number of fusiform bacilli and spirilla. Whether this was a coincidence or not we do not know. In one instance we got a pure culture of fusiform bacilli.

DR. PETER BASSOE: If we were to read up the history of epidemics, we would find that in every epidemic of influenza there have been a large number of nervous complications. As far back as 1740 it was noted in an epidemic that there were many cases of nervous disease characterized by somnolence. In 1889 and 1890 there was an epidemic going over Europe without a marked mortality, but with a complication that was thought to be an encephalitis affecting the brain stem. This was known at that time as "nona," a name that has since been forgotten. In 1918 in England, in Austria and in France, there was described a condition called lethargic encephalitis, characterized by fever, headache, drowsiness, and more or less paralysis of the cranial nerves, particularly the ocular nerves. After a time it was thought to be a form of poliomyelitis, but it had none of the ordinary poliomyelitic symptoms. Finally, it was pointed out by a French surgeon that it was probably an influenza infection. The mortality was given as, I think, 25% in England and 35% in France. Now in the last few weeks there have been a number of such cases in Chicago. I myself have seen six. Dr. Tieken has seen six or seven. These cases have all been very much alike, characterized by very marked drowsiness, no cell increase in the spinal fluid, no headaches, and more or less cranial paralysis. I have seen some of the patients brought in with a facial paralysis and some with an ocular paralysis. I have a couple of cases under observation now. They show a marked rigidity which is similar to the rigidity we see in paralysis agitans. I think it is wise for us to be on the lookout when patients who have had influenza become very drowsy and then develop cranial nerve paralysis.

E. O. JORDAN: I should like to say just a word about some of the observations on the bacteriology of the epidemic as it bears on what has been said in regard to the different types in different sections. In our group, section B, where there were 92 cases, we very rarely found the influenza bacillus in any of the smears throughout this epidemic. They could be found in a few cases by searching very carefully. At the same time, in October, in the cases obtained from the hospital, this bacillus was found in considerable numbers. In this case it would seem to be a group affair. As to death rates, Philadelphia and Baltimore seemed to have much higher death rate than other large cities. New York and Boston had lower rates. Some cities in this neighborhood, Milwaukee, St. Paul and Minneapolis, had lower death rates than Chicago.



Feb 1917. E. Fletcher Ingals M.D.

EPHRAIM FLETCHER INGALS

1848-1918

Dr. Ingals was born in Lee Center, Lee County, Ill., Sept. 29, 1848. His father came to that place as a pioneer from New England and the family endured the rugged hardships incident to opening up the wilderness in those early days. This early experience had much to do with the formation of character and habits which made his career successful in his profession. His father and mother were sterling Christian people, hard working, and successful in winning by their own and their children's labors a living from the fruitage of the soil. Young Ingals bore his share of these burdens, but secured an education in his winter's schooling and in Rock River Seminary at Mount Morris, Ill. He was fortunate in having an uncle, Dr. Ephraim Ingals, in active practice in Chicago, and under his inspiration and advice came to live with him and to attend Rush Medical College, from which he graduated in 1871. He immediately secured an internship in Cook County Hospital and afterward entered practice. His hospital experience and his subsequent work in general family practice were invaluable as preparatory to his special field which was to be his life work—laryngology.

Sept. 5, 1876, he was married to Lucy S. Ingals, daughter of Dr. Ephraim Ingals. Of the seven children, four are now living: Francis E. Ingals, Woodruff, Wis.; Melissa Rachel (Mrs. Clarence L. Fisher), Lyons Falls, N. Y.; Ephraim Fletcher Ingals, Jr., recently in the aviation service of the army, and Mary Goodell Ingals, a student in Rush Medical College.

An aid to his development, also, was his immediate entrance on teaching in the college. It is interesting to note with what a high sense of responsibility he looked upon his duties at this time. In an address given at a dinner tendered him by his colleagues, April 28, 1913, when a loving cup was presented, he said, "I resolved to take up the burden where he (his uncle, Ephraim Ingals) laid it down and to do all that in me lay to make Rush Medical College one of the foremost medical institutions in this country. I had no money and few acquaintances and I realized that success in this undertaking depended on my 'making good' in the profession; therefore, my every effort was made with this ulterior object in view." With singular

devotion to this ambition, he did "make good," and lived to see his dream realized. Those who knew him intimately, can recall his unselfish, constant, persistent labor for that end. The union of the college with the University of Chicago for which he worked indefatigably was the culmination of his dream, and for which he was largely the instrument; for he, first, sought President Harper and opened negotiations with him for the purpose of bringing about this union.

In 1878, the American Laryngological Association was founded—the first national society of laryngology of modern times. He was a charter member. He had already entered on the practice of laryngology and diseases of the chest. And here he was among his peers and personal friends to whom he always gave his best. His position as lecturer on diseases of the chest and physical diagnosis (1874-1883) and his subsequent position as professor of laryngology in Rush College afforded him wonderful advantages, which he used with heart and soul for many years. He soon became an authority, recognized in this and foreign countries. Among his confrères he was honored because of the value of his opinions, and in discussion he was listened to with attention. He held his views tenaciously when he had once formed an opinion.

We think it not too much to say that to him must be given the credit of having taken the first steps in the formation of the Institute of Medicine. He had long had in mind a society of somewhat the same character, and at first worked and talked for an academy of medicine for some four years before the Institute was started. He called a meeting of a few of the leading men in the profession at the University Club in 1914, at which time the formation of the Institute may be said to have been initiated.

He early began to contribute to the literature of medicine, chiefly in his own specialty. More than 150 articles are scattered through the transactions of the various societies of which he was a member, and in the numerous periodicals of this and European countries. His last contribution was an article on angina pectoris,* finished while he was lying in bed during the closing period of his life. It was a brave and characteristic thing for him to do—to use his own illness as a text for a discussion that might be of benefit to humanity—regardless

* Ingals, E. Fletcher: Angina Pectoris, Proc. Inst. of Med. of Chicago, 1918, 2, p. 50.

of the fact that he well realized that his end might come at any moment; so sensitive was he to the demands of what he considered his duty. He died in a paroxysm of angina, April 30, 1918.

Dr. Ingals was inventive, and many things he did were noteworthy. At the last meeting of the American Laryngological Association which he attended, in 1917, he again claimed and established his claim to devising a unique and successful intranasal operation for drainage of the frontal sinus through the nasal passage. The efficacy and safety of the operation in his hands he stoutly maintained in this paper. An instrument devised by him for the application of a wire snare about nasopharyngeal growths some years ago was a very useful instrument. He devised many other instruments. His work in bronchoscopy was noteworthy. Among the earliest to take up this new method he soon had an adequate equipment, many of the instruments invented or adapted by himself. This work he pursued with the same quiet, constant persistence and ardor so characteristic of his work always, up to the time of his taking his bed in his final sickness. Even at the very last, he hoped he might still be efficient in this work: "if he could lie down until all the instruments and patient were ready, and then himself do the bronchoscopy, and then lie down again"; such was his courage and devotion. These are but examples of the things he did. During the later months, when death often seemed very near, he said that when he could not be efficient he wanted to die.

A most useful contribution was the Treatise on the Chest, Throat and Nasal Cavities (1881) which passed through several carefully revised editions and was a most valuable textbook.

Dr. Ingals allowed nothing to interfere with his professional work. To that he had devoted his life. In his long hours in his office no moment was lost. He had little time to spend socially with his patients. Each spare moment was utilized with something connected with his professional work—the preparation of articles, devising of instruments, plans for college work, etc. He often said that one who entered the profession should give all of his time to it, and he often advised young men in the beginning of their professional lives to give themselves wholly to it. In the days of scant practice there were books and journals to be read, dispensary, charity and hospital work to which they could give time and strength, and thus prepare them-

selves for the future and the success which would be sure to come to them if their devotion to their profession was thus exercised.

We would pay our tribute to one of the best helpmates a man ever had, in the person of his devoted wife, who sympathized with and joyfully joined in the tasks and sacrifices that confront such men as he.

The attributes that made Dr. Ingals what he was as physician, teacher, organizer, citizen and friend are not far to seek. He came of good stock. His people were stable, thoughtful, honest, hardworking folk. His parents were of necessity frugal and selfdependent, and he learned those lessons from them. His education was a lifelong process and he kept abreast of the best thought in his profession, and was ready to adopt that which was of proved value. The discoveries in tuberculosis led him to send a special student to Germany to learn at first hand their value. He at once recognized the value of cocain in his specialty, and we can well remember his enthusiastic forecast of what it would mean in the surgery of the nose and throat. We remember also his caution in the acceptance of diphtheria antitoxin, until he was convinced of its value. He could not submit his patients to experimentation. It is refreshing, in view the grandiose flare that is so much the fashion of our time and the waste of energy in spurts of ostentatious efforts, to see a man go about the purposes of his life with quiet continuity, succeeding steadily, making but few mistakes. He succeeded by no haphazard process, but by persistency, and often with compromise.

This persistency in effort made it possible for him to accomplish a vast deal of work without hurry, even with great deliberation. He would make every minute of his working day count, whether it might be in the care of his large practice with which his office hours were often crowded to the utmost; his college work, which he never allowed anything to interrupt; his medical writing which usually had to be done at odd moments in the daylight hours (for he was not one of those who could dispense with his eight hours rest at night), or his secular business.

He was methodical in his habits. His many case books are evidence of his careful diagnosis, his painstaking record of symptoms and prescriptions, and the progress of the case at each succeeding visit. The young men who became his office assistants have much to be thankful for in the careful training they received in his office.

These records formed the basis of much that he wrote in after years. His work was thus free of the slovenly hit or miss faults that are so common among physicians.

He was an unusually good practitioner. He inspired his patients with confidence. No emergency found him unprepared. His self-poise was remarkable, and in the most critical conditions he went about his work, coolly and unafraid, and seemed able to muster with calmness all his knowledge and skill for the event of the moment.

His long years of service as comptroller of Rush College were invaluable. Here his careful business methods, which had made for his personal success, established for the college a reputation that recommended it to the business world and undoubtedly helped to secure the large contributions recently given for the development of the undergraduate school of medicine and the Rush Postgraduate Medical School of the University of Chicago.

Dr. Ingals was a generous man. With his careful education in thrift in youth, often evident in his business dealings, he was the soul of honor, and his word was inviolable. His charities were unostentatious. For many years he set aside 10 per cent. of his income for such use, and from this fund he gave freely and carefully. One incident in the knowledge of one of us shows clearly his generous impulses, and is gratefully recorded here: A medical student in his junior year was stricken with typhoid fever. Dr. Ingals was called. The boarding house in which he and his wife were living was not a good place in which to be ill. The student wished to be taken to a hospital. "Wait until tomorrow before deciding," said Dr. Ingals. He went home to talk it over with Mrs. Ingals, and then his own room was given up to this student and his wife, and he was tenderly cared for, for many weeks, and nursed back to health and strength under the Doctor's and Mrs. Ingals' sympathetic and kindly care. This kindliness of his nature was not worn on his sleeve, but was hidden in his heart and known to those who knew him well.

We delight to honor him for having lived the best that was in him. He was not a genius, except that he had a genius for hard, persistent effort. He had high ideals to the accomplishment of which he had a life-long devotion, which never wavered. He was not an orator, yet he overcame a native diffidence, and no one was listened to with greater respect, and he never hesitated to defend his opinions with his simple, plain and often eloquently convincing way. He was

not a literary man, and yet his contributions to medical literature and articles show careful thought, expressed in simple but vigorous language.

Dr. Ingals "made good" not in any spectacular way, but he died after a long life of constant, persistent, painstaking devotion to the duties of every day as they presented themselves. Honored and esteemed by his fellowmen everywhere, he fell asleep, after a well rounded and very useful career of seventy years.

JOHN EDWIN RHODES,
NORMAN BRIDGE,
STANTON A. FRIEDBERG.

THE INSTITUTE OF MEDICINE OF CHICAGO

PRESIDENT'S ADDRESS

JULIUS STIEGLITZ

December 3, 1918

Tonight the Institute starts on the fourth year of its existence. As retiring president I was slated in our original program for this evening to address you on the topic of "Chemistry and the War." But now, the war is over and in the immense relief of the strain of great efforts and great anxieties we are all war weary and eager to find new strength, new vitality in contemplating fields of activity more attractive, more constructive, more hopeful of achievement without concomitant misery. We are fortunate, therefore, in the fact that our honored guest from the most famous medical institute in the world will deliver the real presidential address this evening on a subject much more to the heart of every one of us and especially of myself than the questions of poison gas warfare, the manufacture of explosives, of millions of shells, and other horrors of the nightmare, all too real, from which the world is just now awakening. I feel the easier in thus unburdening myself of a formidable presidential address by recalling to you that only a few weeks ago I had the pleasure of addressing you at length on the subject of "Chemistry and Medicine." But before proceeding to the important part of the program for the evening, I wish to use this last opportunity to command your attention for the purpose of discussing two or three matters of intimate concern to the Institute.

During the current year we have simply marked time: this had to be so, with so many of our members in service, abroad, in our camps and in Washington, and with those of us who remained here working at 150-200% of our normal capacity, to contribute to the limit of our ability, dutifully if inconspicuously, to the full development of our nation's strength. We have marked time in common with all the other great scientific bodies the world over. But now, with the dawn of peace, we must turn with renewed ardor and vigor to the accomplishment of those ideals which led to the founding of our Institute. And foremost in those ideals, I take it, strengthened as never before

by the lessons of the war, is the desire to advance by every possible means the discovery of new medical truth by painstaking, tireless research. What can we do actively to stimulate research that we are not now doing? In the first place, I would suggest for the consideration of the governors the proposition made by one of our members, Dr. Le Count, that the Institute endow research fellowships. It is indeed one of the great needs of the day to capture and hold the imagination of ardent young men of ability and ideas in the field of medical research before growing practices leave them but a tithe of their vitality and strength for the problems of experimental medicine. One or two fellowships of $1,500 to $2,000 would represent prizes for the most ambitious of young men whose dreams of productive work would otherwise be killed outright by the cold facts of the need for self-support.

Another active measure which I trust our governors will consider is the inauguration of a specific high honor by the Institute, such as a special lectureship, like the Faraday Address in London, or a gold medal to be awarded annually or only on special occasions. Speaking only of local medals, we have the Willard Gibbs Medal of the Chicago Section of the American Chemical Society, which has brought to our young men the stimulus of hearing and seeing in person some of our greatest chemists, foreign as well as American. And we have the medal of the Geographical Society of Chicago, which has brought to our city Peary, Nansen and other great contributors to the earth sciences. Why should not the Institute of Medicine endow, say a Pasteur medal in honor of the great founder of modern medicine, an honor which well might be prized by the greatest of our living contributors to the most blessed science in the service of man?

In the coming year the governors of the Institute will, I trust, give much serious consideration to such plans as these for the active encouragement of research: a committee has already been appointed to study these possibilities, a committee which will now become active since the burden of war has been lifted from our shoulders.

The Institute, I believe, is also going to be more active than ever in the study of civic problems of medical interest by committees of experts, developing our full and splendid strength in that direction along the lines followed so successfully by the committee of Dr. Pusey on control of the social diseases. To neglect to give our city the

benefit of nonpolitical, unbiased advice of experts in such matters as milk supply, medical care of schoolchildren, quarantine and adequate support of our health activities would be to neglect what seems to me the highest duty of our Institute. Committees have been appointed to deal with some of these problems and with the fair prospect of peace, they should become active at once.

Finally, the third purpose of the Institute to secure a home, a comfortable meeting place for its membership, is also an important one from the point of view of stimulating progress by research: I am sure many of us, older members as well as young men, regret that at these our formal meetings opportunity for quiet informal discussion of scientific problems, of medical points of view, of civic needs, are all too meager. Nothing is more stimulating to research than is cross-fertilization of ideas, than the impetus received from a suggestion in informal discussion with a friendly critic. All these valuable results would accrue to us if we could seek inspiration, sympathy, criticism, an occasional douche of cold water, if you will, from the friendly intercourse in a home of the Institute.

I am hopeful, therefore, that while we have done no more than to mark time during the current year, we shall now take up the problems of the development of the Institute to the full power of its inherent possibilities with renewed ardor in the year we are opening tonight. May I add that it might be wisest to invest first in men and brains, to attempt to accomplish first what is in easy reach, while we are maturing the plans and developing the opportunities for our more expensive undertakings.

And now, having dutifully paid my respects to the august office of president of the Institute, I turn with heartfelt pleasure to the important feature of our program of this evening. In welcoming and introducing our guest of honor, I have the threefold pleasure and honor of introducing a representative of France, that glorious country which in our time of greatest need helped us achieve our country's independence, a representative of the French army, that great and brave army that sustained for four years the shock of overwhelming forces of organized and prepared militarism; that brave army that was no less staunch and self-sacrificing in the dark days of threatening disaster before an exultant, arrogant foe, than it was self-sacrificing and alert when at length the tide turned and the most marvellous

campaign of all times was launched and carried to its brilliant end by the allied armies under the masterly leadership of General Foch. And, finally, our speaker is a representative of the Pasteur Institute, that monument in honor of the great founder of modern medicine, Louis Pasteur, of whom I like to think as the noblest of the many great gifts which our science, chemistry, has given to medicine. I have the honor of introducing to you Dr. Etienne Burnet, Major in the army of France.*

* Dr. Burnet's address will be published later.

INDUSTRIAL POISONING IN AMERICAN DYE MANUFACTURE

ALICE HAMILTON
Hull House, Chicago
March 1, 1919

The introduction of the manufacture of coal tar dyes into this country has involved the production and use of a very large number of compounds which are more or less poisonous, and which, up to the breaking out of the war, were not made in this country, and were not even imported for use except to a limited extent. Since 1914, benzene, toluene and xylene have been produced in coke by-products works and in gas works to an increasing extent, and they are rapidly displacing the less toxic petrolatum products as solvents for fats, gums, rubber, in addition to their use as starting points for the manufacture of dyes. As a result, benzene poisoning, which only a few years ago was almost unknown in this country, is now of fairly frequent occurrence, while a whole series of new and unfamiliar poisons are being produced each year from benzene or its homologues, especially in the dye industry.

The coal tar residuals used in dye manufacture are benzene, toluene, xylene, naphthalene, anthracene, phenanthrene, and carbazol, all formed on the benzene ring. The first three are decidedly toxic, though the entrance of a methyl group into toluene makes it less toxic than benzene, and xylene with two such groups is still less so. Naphthalene is very slightly toxic, and the last three seem to be quite inert. The derivatives of these bodies which are used in making dyes chiefly are the nitro, amido, chlor, chlor-nitro, amido-nitro, hydroxyl, carboxyl, and alkyl compounds.

In face of the bewildering complexity of compounds with which one is confronted in this trade one naturally tries to discover some broad principles of physiologic action based on chemical structure, in order to simplify the problem somewhat. Unfortunately, such a simplification is possible only to a limited extent, for the toxicity of a body does not depend wholly on its chemical constitution. Anilin and benzidin are very closely related, but anilin is a volatile liquid, easily absorbed through the skin, benzidin is a solid, not volatile, and apparently not absorbed at all through handling.

There are certain chemical groups whose entrance into a compound of the benzene series does alter its toxicity fairly uniformly, although there are exceptions to every statement made on this point. For instance, one of the most frequent reactions used in dye manufacture is sulphonation, the introduction of the SO_2OH group. This changes a toxic into a harmless body. As soon as anilin has been sulphonated one need pay no more attention to it. The acetyl radicle — CH_3CO — has the same effect though not as markedly. Acetanilid is still poisonous, though not nearly so much so as anilin. The introduction of the COOH group also lessens toxicity. Nitrobenzene is very toxic, nitrobenzoic acid is harmless, phenol is toxic, salicylic acid is far less so.

On the other hand, toxicity is greatly increased by nitration, the introduction of the NO or the NO_2 radicle, the nitro and nitrochlorbenzenes are much more poisonous than the benzenes and chlorbenzenes. The HO group increases toxicity, pyrogallol which is trihydroxybenzene, is more poisonous than phenol, monohydroxybenzene. Chlorin is the only halogen of any importance in the chemistry of dyes. It greatly increases the narcotic effect of compounds of the fatty series, but does not alter the toxicity of the benzene series. The entrance of an alkyl group, methyl, ethyl, etc., lessens toxicity.

No rule can be given as to the comparative poisonousness of the isomers. The Germans think the para position is on the whole the most toxic and the ortho least, but there are ever so many exceptions to this rule.

There are certain fundamental processes which are employed again and again in dye making, and which involve the use of organic and inorganic compounds, some of them distinctly poisonous.

1. *Sulphonation.*—This is done with fuming sulphuric acid, usually added in excess, and the danger comes from the acid fumes and the fumes from the substance to be sulphonated. Benzene is sulphonated in the course of phenol manufacture, anilin is sulphonated as a starting point for many reactions.

2. *Caustic fusion,* usually of a sulphonated product, in order to replace the SO_2OH group with an HO group, as when benzenemonosulphonic acid is changed to phenol. The danger here is from the caustic, and severe burns, especially in the eyes, are not an infrequent accident in connection with this process.

3. *Nitration.* Mixed nitric and sulphuric acids are used, so that the sulphuric may take up the water liberated in the course of nitra-

tion. The danger here is the one always present when an organic compound is in contact with nitric acid. "Nitrous fumes," a mixture of the oxids of nitrogen, are always formed to some extent, and often there is an accidental decomposition leading to excessive production of these oxids. This is the accident which was specially dreaded in connection with the making of explosives, all nitrated products. In dye manufacture the acid used is not so strong, nor are nearly as great quantities needed as in making explosives.

4. *Reduction or amidation* — the substitution usually of NH_2 for NO_2. This is effected by iron filings and hydrochloric acid. The most familiar instance is the reduction of nitrobenzene to anilin. Here the danger lies not in the process, but in the fact that both compounds are poisonous. Owing to the way it is done the danger of anilin poisoning is much greater than of nitrobenzene.

5. *Chlorination.* Fumes of chlorin gas are a danger here if not carried off by strong exhausts. The chlorination of toluene to form benzyl chlorid and of anilin to form so-called anilin salt are the two commonest processes under this head.

6. *Alkylation* — the introduction of methyl or ethyl radicles into a hydroxyl or amido group. Dimethylanilin and diethylanilin are very important dye intermediates, used in great quantities, and their production has given rise to much poisoning. They are less toxic than anilin, and many of the cases of poisoning are doubtless caused by the anilin, but others are attributable to the finished compounds themselves. Ethylation is not attended with any danger save from the anilin, but methylation involves the use sometimes of methyl alcohol, never a safe thing to handle, sometimes of dimethyl sulphate, which is extremely toxic. Both in Germany and in this country this is regarded as one of the most dangerous bodies used in the dye industry. It is not essential, ethyl alcohol or chlorid will do the same work, but they require great heat and pressure to bring about the same reaction that can be obtained with dimethyl sulphate without great heat or pressure.

7. *Oxidation.* Usually inorganic salts are used for this, potassium bichromate, or permanganate, or chlorate, or lead oxids, with a mineral acid. The one that gives the most trouble is potassium bichromate. "Chrome ulcers" are fairly common among men engaged in oxidizing anthracene to anthraquinone.

8. *Diazotizing.* An amido compound on treatment with nitrous acid (sodium nitrite and hydrochloric acid are generally used) yields

a compound called a diazo. This is then coupled with an aromatic amin or phenol to form an azo compound. The azo dyes, a large and important class, are produced in this way. The reaction takes place at 0 C., so the danger is only in handling the bodies that are to be diazotized or coupled.

It is not necessary to describe the symptoms of poisoning from benzene or from its nitro and amido derivatives, for they are very familiar by now, though only two years ago they were still known to few physicians outside the industry itself. Even now there is some confusion as to the mode of entrance of these poisons, and therefore of the proper way to protect the workers, but the evidence is rapidly accumulating of both fume poisoning and skin absorption. The instances I have gathered of poisoning from these compounds are all from American sources. Nobody can study this industry without going to German sources for most of the toxicology and all the chemistry, but it is never safe to assume that the processes carried on in German factories will be the ones used in American factories for American industry always differs in many respects from European.

Benzene poisoning, as it occurs in dye works, is not the slower form, with purpura hemorrhagica and extreme anemia of the aplastic type, such as has been described by Selling[1] among cannery workers, and by Harrington[2] among rubber cement workers. In making dyes, exposure to benzene is an accident, not an incident of the usual work, and the poisoning is rapid and severe, resulting in sudden loss of consciousness and, not infrequently, death in a few hours from respiratory failure. The effect is very quick and intense. Men who must repair pipes, or stills, or storage tanks, or who must watch a stream of benzene flow from a pipe, or who work near a leaking pipe, become irrational and excited, then lose consciousness, and, unless given stimulants and oxygen promptly, succumb to the poison in a short time.

The action of the nitro and amido derivatives of benzene differs from that of benzene. No such leukopenia is seen in poisoning from anilin or nitrobenzene. Methemoglobinemia is characteristic of these forms of intoxication, and in the urine, which is always darker in color, methemoglobin has been demonstrated, although urobilin and hematoporphyrin are more usual. In connection with the urine of anilin workers one must not omit to mention the occurrence of bladder

[1] Johns Hopkins Hosp. Bull., 1910, 21, p. 33.
[2] Boston Med. and Surg. Jour., 1917, p. 293.

carcinoma which the Germans have found to be disproportionately prevalent among them. Whatever the substance responsible for it, apparently it is an amido, not a nitro compound. Nitrobenzene workers do not have bladder tumors, anilin workers do.

Industrial poisoning takes place chiefly through the skin. A few instances from American factors will show how little is needed to produce serious symptoms when it is spilled on the skin.

An elderly man was carrying nitrobenzene in a drum and spilled some on his clothing. Almost at once he began to stagger and spilled some more, then he suddenly collapsed on the ground. They did not strip him but sent him in his working clothes to the hospital where he died within an hour of his entrance there. Two men were set to cleaning out the iron filings from an anilin reducer, one working with bare hands, the other with canvas gloves which became soaked. Both were poisoned, the one with gloves being incapacitated for two weeks, the other for only five days. A foreman in an anilin plant was doing experimental work and got anilin on his hands and was careless about washing. One morning he complained of headache and by noon was so ill that he went home, but without washing his hands. At home his symptoms grew alarming and a doctor was sent for who found him vomiting, his pulse very weak and his color cyanotic. Shortly after, he had a convulsion, sank into unconsciousness and after another convulsion his heart grew steadily weaker and he died in less than 18 hours after being taken sick.

Fume poisoning does occur, but not so frequently. A severe case of cyanosis and heart weakness was sent to a hospital in Brooklyn, the man having climbed a ladder to look into a boiling vat in which there was dimethylanilin, and inhaled the fumes. I have one case of industrial poisoning from swallowing anilin, a chemist who was syphoning anilin from one drum to another and drew it up into his mouth. He thought he spat it all out and he rinsed his mouth well, but in an hour symptoms of poisoning came on.

Of the compounds derived from anilin and nitrobenzene, the ones that have caused most serious poisoning in our dye works are paranitranilin, the nitrochlorbenzenes, dinitrophenol and alpha-naphthylamin, which is derived from naphthalene by amidation just as anilin is derived from benzene. To take the last first, there were five cases of accidental poisoning from excessive fumes of alpha-naphthylamin a couple of years ago in Perth Amboy. The men were employed on the night shift in a plant making naphthionic acid, a sulphonic derivative from alpha-naphthylamin. The chemist was not there and they guessed at the quantities of sulphuric acid and alpha-naphthylamin, with the result that the tank boiled over and they were all exposed to the fumes. One man recovered promptly, a second has left the place

and his history cannot be traced. Two were taken to the hospital, one two days after the accident, when he had a temperature of 101 F., was jaundiced, vomited bile-stained fluid, and passed with difficulty urine which contained much blood. He recovered, but the fourth man who also went to the hospital, after having been treated at home for two weeks for supposed typhoid fever, died there on the 4th day, his blood showing an extreme degree of destruction of red corpuscles. He was delirious, very weak, his liver and spleen enlarged, vomiting and diarrhea were continuous, the urine contained albumin. The fifth man has never recovered his health entirely since then. At the time he suffered from pain in the kidneys and bladder, passed urine that looked like pure blood, was incapacited for three months with weakness, headache, dizziness.

Only the other day I was told by Dr. Alfred Stengel of Philadelphia of a man who came to his clinic with a hemoglobin of only 20%. He gave a history of having been poisoned some three months before by a single exposure to an excessive amount of paranitranilin dust in the course of screening it, after which he quit the job and had never been exposed to paranitranilin again. He was given three transfusions of blood which brought about no improvement at all and he died shortly after. Levine[8] describes a case in the great dye works at Hoechst. A man who died after only 5 hours' exposure to paranitranilin dust.

Many of the most poisonous of these compounds set up a very distressing dermatitis when they come in contact with the skin. This is especially true of the chlor- and nitrochlorbenzenes, the nitranilins and the nitrophenols. It is really in a way an advantage to the workman that this is so, for it tends to protect him from more serious forms of poisoning. A man will endure systemic symptoms of poisoning when he will not endure an itching, burning rash, and consequently manufacturers are sometimes faced with so great a labor shortage because of the irritation from these dusts that they are obliged to use mechanical means of getting rid of it, and incidentally the men are protected from more serious damage.

The dinitrophenols are intermediates for certain dyes and are formed at one stage in the less usual method for the manufacture of picric acid dinitrophenol. This is the method used by the French and also by three American factories. Dinitrophenol poisoning was prev-

[8] Ztschr. f. Gewerbehygiene, 1909, p. 597.

alent enough in French munition works to give a great deal of trouble, and though we had handled it only a short time and only a few men were exposed to it, there were found deaths from dinitrophenol poisoning last year. Three were rapid and acute, the men having been exposed to an unusual amount of the powder. The symptoms, as described by the French,[4] are vague at first, then the temperature rises rapidly to 104 F. or over, there is great nervousness, sweating and thirst. Uremic symptoms then come on, convulsions and coma. The changes in the organs are not characteristic. The fourth American case was slow in onset and the man apparently died of toxic jaundice, as have so many of the victims of trinitrotoluene poisoning and of the so-called "dope poisoning"— tetrachlorethane. This case was reported by Warthin,[5] who examined the urine and liver. He found abundance of bile pigments in the urine and the tests for phenol derivatives, both nitro and dinitro, were strongly positive. The liver was grass green, the capsule shrunken, lobules small. Microscopically, the picture was that of an acute degenerative hepatitis, such as is found in acute yellow atrophy of the liver.

There are a few compounds used in dye manufacture which do not belong to the benzene ring, but which are very toxic and are regarded with unusual apprehension by the men in the industry. Hydrogen sulphid is one of these. It is used largely in the manufacture of sulphur dyes as a reducing agent and in case of accident the escape of this gas gives rise to sudden and grave poisoning. Hydrogen sulphid is dangerous in less than one part per thousand parts of air and one part and a half may be fatal. The danger is especially to be apprehended in making of sulphur browns and yellows and in these factories great precautions against accidental escape of the gas are taken.

This is a very incomplete description of the poisons encountered in the dye industry, and though I cannot hope to make it anything but incomplete I want to add one more compound before closing, namely, phosgene. This gas is familiar to us all from its use in gas warfare. In industry it is important as producing, when treated with dimethylanilin, Michler's ketone, or tetramethyldiaminobenzophenone, which is used for many dyes. Phosgene gas has already caused at least three deaths in the dye industry, perhaps five. It is interesting

[4] Martin, E., and Guerbut, M.: See abstract in Monthly Labor Review, U. S. Bureau of Labor Statistics, Aug., 1918, p. 242.

[5] Bull. International Association Medical Museum, 7, p. 123.

to note that these industrial cases show the disastrous effects of exertion after inhaling the gas, just as the military cases did. There were a number of workmen in one plant gassed by the accidental escape of phosgene, but all were given prompt treatment and recovered. An Italian teamster who was outside the building and was not known to have inhaled the gas, was allowed to go on working and then go home. He died shortly after reaching home.

THE HUMAN MACHINE IN THE FACTORY

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In the year 1913-14 the Marey Institute, the prominent physiologic institute of France, conceived a plan for the investigation of the general problem of industrial fatigue. The coming on of the war prevented a realization of the plan. But the coming on of the war did exactly the reverse in England. In 1915, Mr. Lloyd George, who was then Minister of Munitions, appointed the Health of Munition Workers Committee, consisting of scientific men, representatives of industrial plants, and government officials. The committee took up the investigation of industrial fatigue and allied problems, labored diligently for three years, published valuable reports, and went out of existence in 1918. Its place was taken by the Industrial Fatigue Research Board, under the chairmanship of Professor Sherrington, and further extensive investigations are already being performed.

In 1917, soon after we entered the war, the United States Public Health Service also undertook the investigation of various topics relating to the work of the human machine in the factory, being assisted in an advisory capacity by the Divisional Committee on Indistrial Fatigue under the Committee on Labor of the Council of National Defense and the similar Committee of the National Research Council. Our work is still being carried on, and we have a very considerable program for its continuance.

What I have here to report consists largely of the results of the work that has thus been done in England and in America during the war.

It has been believed by both the English and the American investigators that in a properly conducted study of this kind only exact scientific methods should be employed, and accordingly the endeavor has been made to secure, so far as possible, results in terms of quantitative measurements. A number of technical physiologic methods have been used for the detection of fatigue and for other purposes, but since most of these methods have been found to be of limited and uncertain use, I will mention only three. These are: the spring-balance method of determining muscular strength, the vascular skin reaction test, and the cinematographic method.

The spring-balance method was devised by Prof. E. G. Martin for the determination of the strength of muscles partially paralyzed in poliomyelitis and the gradual restoration of their power. It consists in measuring in pounds the force that is required to overcome the contraction of certain selected groups of muscles and computing from the figures thus obtained the total strength of the body. The test affords a valuable index of bodily condition. By this method it has been found, for example, that the strength of the individual often diminishes during the working day, particularly in the more severe operations and with the weaker workers. It has been found, too, that the different operations in the factory require different standards of strength. Thus, the standard strength in the operation of "rivet dipping" is 4,870 pounds, in "coal passing" 4,230 pounds, in "powder loading" 3,700 pounds. The strength shown by women is markedly less than that shown by men. By means of the test, workers can be classified, and the economic disadvantage can be avoided of assigning the strong worker to the weak job and vice versa.

The vascular skin reaction test was devised by Prof. A. H. Ryan. By means of a suitable apparatus a stroke is made across the skin of the forearm. This causes after a few seconds a white dermographic streak to appear, which increases in intensity and then gradually fades away. The time that elapses between the making of the stroke and the termination of the maximum whiteness of the streak is shorter in fatigue. An index of fatigue is thus obtained, and a diurnal curve of fatigue may be plotted. This shows, for a working person, a fall during the forenoon, a cessation of the fall or even a slight rise during the luncheon period, and a further fall during the afternoon. Interpreted in physiologic terms the curve reveals the progressive course of fatigue during the two spells of the day's work and the interruption of the fatigue process, or even a partial restoration of working power, during the luncheon period. The degree of fatigue appears to be proportional to the output of the worker. A night's sleep or a Sunday rest restores the working power completely.

The cinematographic method has been used in both France and America to present in graphic form bodily positions and bodily motions. It makes it possible to analyze complicated motions into their components. It indicates the differences between the skilled and the unskilled worker. Amar has combined advantageously the cinematographic method with a method of tambour registration of physiologic

movements, and has thus demonstrated among other facts the greater rhythmicity of the skilled worker's motions.

A method that has been used extensively both in this country and England is that of measuring the output of the worker. This can be done very exactly in many factory operations, and only exact measurement, with conditions carefully controlled, is here of value. Studies of output may be profitably supplemented by the technical physiological tests.

The diurnal course of output has been studied extensively by the American observers and is illuminating. It may be represented in a graphic curve, which varies according to the type of work but with each type is fairly constant. In one of our large munition factories, engaged in the manufacture of fuses for explosive shells, where the working day was of 10 hours' duration, from 7 a. m. to 6 p. m., with a luncheon rest of one hour, from 12 m. to 1 p. m., the diurnal curve of output in a dextrous operation, requiring careful attention and exact neuromuscular coordination, was found to be as follows: Beginning rather high in the morning the curve rose still further and reached its highest point during the second hour of the forenoon; thence it fell gradually until the luncheon period; beginning at a slightly higher level after luncheon it again rose momentarily, but only slightly, and then fell progressively throughout the rest of the afternoon, reaching its lowest point for the day during the final hour. From such a curve of output certain inferences may be drawn concerning the physiologic state of the individual. The preliminary rise of the curve in each spell indicates the physiologic effect of practice; the fall of the curve in each spell is indicative in considerable part, although not wholly, of fatigue, which becomes more pronounced as the day proceeds. The higher curve just after, rather than just before, luncheon indicates the restorative influence of rest and food. Constant features of dextrous work as revealed by the curves of different operations are the appearance of the maximum of production during the forenoon spell and the presence of maximum fatigue in the final hour of the afternoon spell; variable features include a variable degree of the practice effect and the fatigue, the appearance of maximum production, not always in the second, but often in the third or fourth hour, and a variable degree of the restorative effect of luncheon.

Not all factory operations show an output curve like that of dextrous work. Where the work is of a severely muscular nature there is usually no practice effect whatever, but a marked fall from the beginning of each spell, with a great restoration of working power at the luncheon period. The gradual course of the fall may be interrupted by a momentary spurt toward the end of each spell, but the final minimum is very far below the initial maximum of the day's work.

The pronounced slackening of production that accompanies the day's fatigue and is so common a feature of the diurnal curve inevitably raises the question whether fatigue may not be lessened and the output be maintained more nearly at its maximum as the day proceeds, without at the same time impairing the working power of the worker. This is a question to which much attention has been given by the observers in both England and America. Many devices have been suggested for increasing total output. The very frequent increase that follows the luncheon period suggests at once the possible value of introducing other rest periods. This has been tested in a considerable variety of operations and with a considerable number of workers. In this country we have introduced experimentally two 10-minute rest periods, one in the forenoon and one in the afternoon, in two factories, an 8-hour and a 10-hour factory. The result in the 8-hour factory was rather indeterminate, but in the 10-hour factory it was very definite. Here in 11 out of the 12 operations studied the total output of the day was found to be increased. In one particular case a group of workers in an operation was observed for a number of weeks before introducing the rest periods and then for three successive periods afterward, each period consisting of 2 or 3 weeks. In the first of the subsequent periods the total increase in the day's output was 3%; in the second period it rose to 17%, and in the third period to 26%. This progressive increase was simply the effect of the introduction of two 10-minute rest periods. This was an extreme case, but is very significant. Whole holidays likewise have a beneficial effect. In one factory the stopping of work on the Fourth of July increased the output subsequently by 2%. It will be remembered that more than a year ago the Fuel Administration caused the factories to shut down for 5 days. We determined the daily output in one factory before that period and then for a few days afterward, and found an increase of 8%.

This brings us directly to the question of the proper length of the working day, a question which always obtrudes itself into an investigation of this kind. We have made in this country a comparison of the 8-hour and the 10-hour working periods as they exist in two prominent factories, and have combined in two curves of diurnal output the results in all the operations studied. There is one striking difference between them: Production at the 8-hour plant tended to be more uniform throughout the day, whereas with 10 hours of work the deviations from the maximum were more pronounced, as to both practice and fatigue effects. It might be added that at the 8-hour factory there were fewer absences of workers, and the workers approximated their physiologic capacity more nearly. All these differences attest the greater efficiency of the 8-hour, over the 10-hour factory studied. The facts are suggestive as to the comparative efficiencies of the 8-hour and 10-hour systems, although from two factories alone it would be unwise to generalize. In this connection the data found by Dr. Vernon in certain types of operations in British factories are significant. When there was a reduction in weekly hours in a very heavy operation from 58.2 to 51.2 there was an increase in the output of 22%; in a moderately heavy operation a reduction from 66.2 to 45.6 hours resulted in an increase of 9%; in a light operation a reduction from 64.9 to 48.1 hours caused a diminution in output of 1%. In the heavy and moderately heavy operations the human being was constantly busy — the physiologic element predominated; in the light operation the human being during much of the time watched the machine do the work — the machine element predominated. Thus the living machine works differently from the lifeless machine: with the latter diminishing the hours of labor diminishes output, with the former diminishing the hours of labor, within limits, increases output. Such facts indicate that the problem of the length of the working day has its physiologic features; in fact, it seems to me that it is more a physiologic than any other kind of problem. More investigation is here desired, but such investigation, I predict, will show that the optimum duration of labor varies with both the nature of the operation and the worker: one length of day is best for certain kinds of work and certain workers, and another is best for other work and other workers. The establishment of a universal working day would, therefore, be an unscientific procedure. If it were fixed at 8 hours,

as seems now not improbable, agitation would not stop there. A labor leader said in my hearing in New York several years ago, "When we have secured the 8-hour day, we shall begin immediately to work for a day of 6 hours." American miners are already asking for 6 hours, and in England Lord Leverhulme is advocating the universal 6-hour day. The problem would be clarified if a clear distinction were always made between the length of the workday and the length of the pay-day. Many workers, while demanding the shorter day, are entirely willing to work for the longer time if paid relatively higher wages. The recent grant of the 8-hour day to the railway employees of this country consisted merely in establishing a basic pay day and had nothing to do with the question as to how long railway employees ought to work.

Night work has been investigated in both England and America. Here we have determined the output in certain operations of a factory that maintained a 12-hour night. The work began at 6:20 in the evening, and continued until 6:40 in the morning with a break of 20 minutes for luncheon at midnight. The course of production during the first spell was fundamentally not unlike that of the first spell of day work, the curve showing a practice rise and then a fall; the rest of 20 minutes with food did not prevent a further fall following luncheon; in the second spell there was at first a practice rise followed by a gradual fall; but the most striking feature of the night curve occurred after 5 a. m. This was a precipitate and enormous fall. In one operation where production during most of the hours of the night had amounted to 10 and 11 thousand pieces hourly, it fell during the final 40 minutes to 152 pieces. If the day and night curves of the same operation be compared, the noticeable difference is similar to that between the curves of the 8- and 10-hour plants: greater uniformity of hourly production during the day, and greater deviation from the maximum during the night.

Other facts which we observed in night work were these: The number of seconds that were required to perform a certain specific operation was determined during the four successive 3-hour periods of the night. This time gradually increased as follows: 12, 13.3, 16.5 and 17.4 seconds; that is, there was a progressive slowing of the operation of about 50%. During the early part of the night it is not customary for workers to sleep, but during the final quarter of the

night in the same factory we found 43% of the workers in a group of 74 sleeping at some time. In one factory the night workers were found by the Martin spring-balance strength test to be weaker by 500 pounds than the day workers. Whether this was caused by the work, we do not know.

All these facts indicate that night work is not as efficient as day work, and this is supported by the British observations which show that with approximately equal working periods the output of the night workers was 6-17% less than the output of the day workers. Working at night is and must always be in some degree an abnormal occupation for the human being; but apparently it cannot be dispensed with. The problem, therefore, is how its evils may be mitigated while output is maintained or improved. It seems obvious that the early morning hours after a night of work are relatively unprofitable; that at least the final 2 hours of a 12-hour period might be eliminated and the worker be sent home at, say, 5 a. m., and given more time for sleep. It seems not improbable that by such a change the total production of the night could be increased.

It is well known that the human machine will frequently limit its output voluntarily, in other words, will "soldier." This practice is very common in factories. In one munition factory which we investigated we found it prevalent in more than half of the departments. It is indicated by a constant output day after day or night after night. For instance, one worker on fuses produced at his lathe exactly 1,000 pieces every night for 44 out of 45 nights that were observed; and each member of a group of sixteen workers drilled 3,600 pieces night after night for a week. If a machine breaks down and is stopped for repairs for a brief time, the work is subsequently speeded up and the worker finishes his time with his usual figure. There are many reasons why workers limit their output. A very common cause is the custom of the employer to cut the piece rate when earnings seem to him to approach an alarmingly high figure. When this is done repeatedly, as has frequently happened, the employee recognizes that it is not to his advantage to work honestly up to his capacity. What should here be done and what will be done ultimately, I believe, is to develop a spirit of cooperation on the part of the worker and the employer. The worker should be encouraged to labor honestly and approximate his physiologic capacity, and should be assured that his diligence will be

honestly rewarded. Only thus can efficiency be secured. By physiologic capacity, however, I do not mean physiologic exhaustion. The avoidance of overfatigue is one of the prime essentials of efficiency.

Another topic which has been studied to some extent in both America and England is that of industrial accidents. Most industrial accidents have a physiologic origin: they are due to something that the worker himself does wrongly or fails to do. Of the possible physiologic causes it appears fairly conclusive that fatigue is potent. Accidents increase in number during the working spell, the maximum number occurring, however, shortly before work ceases. The investigators of the Public Health Service find that the accident risk, or ratio of accidents to output, is greatest, at least in the 10-hour plant, in the final hour of the day's work; that is, when fatigue is greatest. Speed of work is probably another cause of industrial accidents; as is also the inexperience of the worker. The latter is indicated by a close parallelism in the curves of the number of accidents and the number of inexperienced workers over a series of months.

This brings up another problem that has been studied especially in this country, namely, the labor turnover, or the constant change in the personnel of the working force. In one of our munition factories there was maintained a force of some 11,000 employees. Nine thousand employees left the establishment during the course of 6 months for reasons unknown to the firm. That is a lamentable condition of things. It has been estimated by Alexander that the introduction of a new worker costs the company $53.92. Thus a large labor turnover involves the employer in an enormous expense, and is one of the factors opposed to a high degree of efficiency. When once efficient workers have been secured every effort should be made to retain them. Here again a spirit of mutual cooperation between employers and workers will be found helpful.

The last topic of which I shall speak is the work of women as compared with that of men. The war increased the number of women workers enormously. During my recent visit to England and France I was greatly interested to learn of the variety of work in which women were engaged. This included such diverse and unusual occupations as lathe-working, wheeling heavy barrows, stoking, butchering, tanning, digging and shoveling. It is remarkable how the British and French women rose to the emergency. But, however laudable such

work may have been for women in the emergency of the war, the question must necessarily be asked whether it is wise for them to continue to pursue all these varied occupations as a permanency. As the war proceeded Dr. Janet Campbell and her assistants made a physical examination of some 2,500 British women workers and found that 42% of them were suffering from fatigue or ill-health. This indicates that many of the women undertook work for which they were not physically fitted. Previous statistics have shown that between the ages of 20 and 55 working women are more subject to illness than are working men, although this is not due to child-bearing alone; and that they are more frequently absent from their work. But there are more profound considerations than these. Just as there are obviously anatomic differences between men and women, I think it must be acknowledged that there are also, although less obviously, physiologic and psychologic differences, which are not the result of education, but are inherent in sex. The lesser muscular strength of women I have already mentioned. If such fundamental differences exist the question of women in industry then is not as to their greater or less general efficiency as compared with men, but rather as to what kind of work women are best fitted for. We must seek to discover the special industrial qualifications of women. It seems to me that it is along this line that the subject of women in industry ought to be studied in the future.

I have thus presented some of the main facts that have been discovered concerning the work of the human machine in the factory. What we are observing here is the rise of what is virtually a new science, a science of industrial physiology. We have established so far merely the beginnings of the science, but I think it is bound to grow. I think, moreover, that, as far as the human machine is concerned at least, science ought to be a guiding influence in the organization and administration of industrial enterprises. The progressive manager appreciates the value and bearing of such knowledge as we have already acquired, and will, I believe, gradually come to make use of it in his treatment of his workers. You are fully aware how grievously during centuries medicine was under the control of empiricism and tradition and how at last science has come to its rescue and changed its aspect. Industry is still under the sway of empiricism and tradition. Science has its mission here to perform, and its success will be as great. In this work of regeneration America has, I believe, a great opportunity for leadership.

REHABILITATION OF THE DISABLED

Frank Billings
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May, 1919

I. REHABILITATION OF THE WAR DISABLED

The world war has aroused a universal interest in the physical and mental rehabilitation of disabled soldiers. The instruments of destruction of modern warfare sacrificed millions of lives and disabled a multitude of men. To conserve man power it became necessary for the European countries engaged in the war to study and apply all possible measures to protect the lives and health of the soldier. The use by the central powers of offensive and destructive measures in the way of high explosives, poisonous gases, liquid fire and other devices produced injuries requiring special measures of prevention and efficient surgical and medical management which could be developed only after careful research and study.

The final year of the war was illuminated by remarkable results of the practical application of known and new measures of prevention of disease, and military surgery reached a stage of technical skill and efficiency heretofore unknown.

EUROPEAN METHODS OF REHABILITATION

In addition to ordinary medical and surgical care, all the European countries engaged in the war adopted measures to hasten physical and functional restoration by the application of special therapeutic measures grouped under the heading of physical and mental reconstruction or rehabilitation.

The program of rehabilitation included physiotherapy, embracing hydrotherapy, electrotherapy and thermotherapy; exercise, passive (massage, mechanotherapy) and active (graduated calisthenics and special training, military drill and games in the gymnasium and out of doors); and occupational therapy in the application of manual and mental training and education in wards, workshops and schools and in gardens and fields. For the soldier still fit for combat or for special military service, convalescent training centers were maintained, where, by means of military drill, instruction in individual and general hygiene, and play, the final hardening and restoration were completed.

All of the Allied countries of Europe together with Canada endeavored to train and educate the soldiers who were so disabled by disease or injury that they were no longer fit for any kind of military service, to qualify them to serve in the civilian industrial army. The rehabilitation program of these countries was carried on through a plan of cooperation of the military and civilian authorities. Limited time and space do not permit one to give here details of the program and the results of rehabilitation of the disabled as practiced by the Allied countries associated with us in the war.

AMERICAN PROGRAM

The United States became engaged in the war so late that our government was able to take advantage of the knowledge acquired by the entente governments by a bitter experience in defensive and offensive warfare, in measures of protection and prevention of injury and death. The Medical Department of our Army shared in the opportunity to apply the newer military medicine and surgery in the prevention and treatment of disease and injury. The program of our government for the care of the soldier and his dependents embraced:

1. The creation of the Bureau of War Risk Insurance, in the Treasury Department, with provisions for voluntary life insurance with the payment of a monthly premium of moderate amount from the soldier's pay; provision for monthly allotment to the soldier's dependent family and provision for the payment of a monthly pension after discharge for a permanent disability acquired in the line of duty.

2. The Medical Department of the Army was authorized by the War Department to include measures of physical reconstruction in the treatment of the sick and wounded soldiers, including the employment of curative work carried to the degree of prevocational or vocational training and education, to fit them for further general or special military service; or if unfit for further military service to discharge them from the Army after the maximum physical and functional result was obtained.

3. The Congress enacted a law approved by the President, June 27, 1918, which made the Federal Board for Vocational Education responsible for the vocational training and education of compensable disabled soldiers after their discharge from the Army.

4. The Congress has provided appropriations and has made the Public Health Service responsible for the hospital care of compensable disabled soldiers who may require treatment after their discharge from the Army.

The policy adopted by the Medical Department of the Army, in the attempt to fulfil its obligations to the government and the soldier, embraced a program of measures of prevention and treatment of disease and injuries, including mental and physical reconstruction or rehabilitation, based on accumulated experience and knowledge.

Advantage was taken of all available knowledge gained by the medical departments of the armies and governmental and other agencies of our Allies. American officers and American hospital units served with the English and French armies before we had developed an army overseas. Hundreds of these medical officers, medical enlisted personnel and American nurses acquired a first-hand knowledge of modern military medicine and surgery, enabling them to give efficient service in our own Army overseas and at home.

ORGANIZATION OF ARMY MEDICAL DEPARTMENT

One of the remarkable developments of the war was the organization of the Medical Department of the Army. Our country was unprepared for war on April 6, 1917. Our Regular Army establishment was efficient but small. The regular Medical Corps numbered less than 500 commissioned officers. As a rule they are a fine and upstanding body of men, many of them well qualified for administrative duty and as surgeons and physicians, a few with world-wide reputation in research work and as sanitarians. At the call of the Surgeon-General the medical profession responded by volunteering for service. The large majority of these men were untrained in military tactics and knew but little of military medicine. But among them were many of the best qualified physicians, surgeons and specialists of our country. The majority quickly overcame the handicap of lack of pure military knowledge and gave service at home and overseas which evoked the praise of the chief commander of the American Expeditionary Forces and of the Surgeon-General. Nor must one lose sight of the spontaneous response of the medical profession to the call of the Provost Marshal-General for service on draft boards, and of the efficient manner in which this service was rendered.

DISEASE AND INJURY PREVENTION

The subject of rehabilitation of the disabled soldier involves the application of measures of disease and injury prevention. The principles involved in the problem of disease and injury prevention as applied to our army were made more difficult by many factors. Men were inducted into military service before the training camps were completed; it was practically impossible to place nonimmune suspects in detention quarters for a sufficient period of observation, and infectious disease carriers thus spread measles, scarlet fever and cerebrospinal meningitis among the susceptible troops. The winter of 1917-18 was characterized by severe cold and much snow, and the newly organized Medical Corps officers were insufficient in number and many were inexperienced at the beginning in how best to deal effectively with the big and difficult problems. In the late summer and fall of 1918 the world-wide severe epidemic of influenza reaped an abundant harvest of lives of soldiers and civilians. A malignant type of pneumonia characteristic of all epidemics of influenza was the chief cause of death. To all of these embarrassments in the application of measures of disease and injury prevention must be added the risk of the transportation of a large army in dense concentration by train in the United States and in France, England and Italy, and in equally crowded ships across the ocean. When overseas the soldiers met a trying climate, more or less uncontrollable insanitary environment of villages where they were billeted, or still worse conditions in the trenches or when advancing and living for days and weeks in a territory occupied by the armies of friend and foe for four years, the soil foul and infected; and finally they had to face a murderous, vicious foe who utilized every destructive element known to science and the devil to kill, wound or maim the opposing army.

But with all these embarrassments, difficulties and universal disability producing causes, the program of disease and injury prevention, and the medical and surgical management of our sick and injured soldiers was carried out by the Medical Department of the Army in a manner so successful that it justified the praise given by the chief commander of the American Expeditionary Forces and of the War Department.

In the making of our Army we selected the best of our young men from a physical point of view. Every man was immunized as a

protection against smallpox, typhoid and paratyphoid fevers by standardized vaccines. Adequate clothing and blankets gave protection to the body. The American military shoe, the product of a research made by a regular Medical Corps officer, made him the best shod man of any army. Military drill and special training, discipline, life in the open, an abundant balanced ration and regular hours soon made an army of upstanding and physically fit men ready for any job. These new soldiers seemed to embody and demonstrate the spirit of patriotism of the nation. Physically and spiritually they had taken over new resistance to disease or injury. These same qualities made them bear disaster, when it fell, with courage and stoicism rarely seen in other men.

Overseas, special centers provided facilities for the correction of defects which were remediable by special training under qualified specialists and put the finishing touch on all. Prevention of combat injury was difficult at all stages of the war, owing to the nature of the weapons and destructive elements utilized by the enemy. Metal helmets and gas masks afforded some protection, but never wholly adequate.

During the last year of the war many lives were saved and in many cases permanent disability was obviated by the employment of efficient medical and surgical care. This modern military medicine and surgery was the outgrowth of the combined experience of the medical departments of the armies of the Allies and the United States, including cooperative research and clinical conferences.

FIRST AID

On the field the well trained medical personnel applied first aid and immobilized fractures with standardized splints carried to the field. This obviated further trauma of the tissues by the bone fragments during transportation to the rear. At evacuation hospitals within the combat zone and often subject to artillery fire, operations including the gravest major surgery were performed within a few hours after the injury was received. Unfortunately, in some battles a difficult terrain or in cases in which the battle was marked by fierce fighting and rapid advance, the evacuation of the injured was necessarily delayed. The soil of "no man's land" was always a source of danger of serious infection to the wounded. Nevertheless, the application of the new

principles of prevention of additional trauma during evacuation from the field by proper fixation with splints, early and thorough cleansing of the wounds, by the removal of all foreign bodies and of devitalized tissues with open drainage obviated to a great extent gangrene and other serious types of infection, which were such a frequent cause of the loss of life and limb in the first years of the war. This explains the relatively small number of permanent disabilities through the loss of legs or arms of our disabled men. The successful application of lung surgery at evacuation hospitals and the life saving result is one of the remarkable events of the last year of the war.

The remarkable results of the treatment of the patients suffering from so-called "shell shock" is due to the application of the knowledge gained by military clinical experience. If this successful treatment had not been applied, thousands of soldiers would have been discharged suffering from types of mental and nervous disability. In the home environment and under the influence of the desire for a pension, many would become permanent invalids—an enormous loss to the industrial world and a continued financial burden to the government.

STATISTICS AS TO DISEASE AND INJURY

In the discussion of the results of the application of measures of disease and injury prevention, I am permitted to quote available statistics. They are subject to correction after all data shall have been definitely verified. The deaths from typhoid and paratyphoid fevers in the domestic forces from Sept. 1, 1917, to March 28, 1919, were 50. In the American Expeditionary Forces from Oct. 18, 1917, to March 28, 1919, there were 146, or a total in the U. S. Army of 196. This gives an annual death rate for typhoid and paratyphoid fevers of 0.06 per thousand. The efficient work of draft boards and of medical examining boards of training camps detected and rejected approximately 50,000 tuberculous men. Pulmonary tuberculosis developed in approximately 11,000 or possibly 12,000 soldiers, of whom 1,036 have died, giving an annual death rate in the whole army of 0.316 per thousand. The total deaths from other infectious diseases were: for meningitis, 2,055, giving a rate of 0.63 per thousand; measles, 119, or 0.036 per thousand; scarlet fever, 163, or 0.051 per thousand; dysentery, 41, or 0.001 per thousand; and empyema, 490, or 0.148 per thousand.

The pandemic of influenza complicated with a malignant type of pneumonia was the chief cause of death from disease in the Army at home and overseas. The medical profession, both civil and military, was unable successfully to institute measures of prevention or cure. The total number of deaths in the whole Army from Sept. 1, 1917, to March 28, 1919, was approximately 39,493, which gives an annual death rate of 11,997 per thousand. During the same period of time the total deaths from disease, including pneumonia, was 48,670, with a rate of 14.797 per thousand. The efficiency of the application of measures of disease prevention and of treatment is shown by the total deaths from disease alone, exclusive of pneumonia, which were approximately 9,177, giving an annual rate of 2.80 per thousand.

The efficiency of modern military surgery is evidenced by the official statement that 85.5% of combat injured soldiers of our Army returned to combat service, and 5% were made fit for special or limited military duty in the rear areas.

The remaining 10% of the combat injured were so severely disabled that death occurred or the nature of the disability made them unfit for further military service. These included the blind, the deaf, patients with amputation of limbs, serious maxillofacial injury, serious peripheral nerve injury, empyema from trauma of lung or pleura, and other surgical conditions.

We may be justly proud of the accomplishments of the Medical Department of the United States Army in the world war. Serious mistakes occurred, due often to uncontrollable conditions and situations. The medical program of hospital construction, supplies, equipment, transportation and countless other needs had to be modified or to wait on other parts of the war program of the government. We know that many mistakes occurred, some serious ones, too, in regard to details, but the whole vast program of the government went through. The end sought was obtained much earlier and more satisfactorily than was anticipated. If the big governmental program had been carried through less expeditiously, perhaps fewer mistakes would have been made in all departments. But had we worked with less haste one wonders whether the Allied armies would now be astride the Rhine.

The policy of the Medical Department for the physical reconstruction of disabled soldiers and later extended to disabled sailors and marines, was formulated in August, 1917, applied in some of the gen-

eral military hospitals early in 1918 and approved by the War Department July 29, 1918. Physical reconstruction was defined as continued management and treatment carried to the fullest degree of maximum physical and functional restoration, consistent with the nature of the disability, by the employment of all known measures of modern medical management, including physical therapy, manual and mental work and recreational play.

To carry out this policy a program was formulated to establish a department of education and a department of physiotherapy in each of the general military hospitals designated by the Surgeon-General to function in the physical reconstruction of disabled soldiers. A division of physical reconstruction in the Surgeon-General's Office was organized, with a director to be responsible for the administration of the work. Subsections on education and on physiotherapy, each with a director, were established in the division.

PERSONNEL OF EDUCATIONAL DEPARTMENT

To establish the educational department with efficient standards the Surgeon-General was fortunately able to secure the services of Dean James E. Russell of Teachers College, Columbia University, to serve as the administrative director. Dean Russell was unable to accept the place permanently, but volunteered to give his services in an advisory capacity for several days of each week in the organization of the educational department. This he did without compensation for the period of five months, when he was obliged to return to his duties at Columbia College. Dean C. D. Coffman of the University of Minnesota occupied a similar position in the office as a volunteer without compensation on the retirement of Dean Russell.

Through the efficient service of these two patriotic men, aided by other qualified general and special educators, who came into service commissioned in the Sanitary Corps of the Medical Department, the Surgeon-General was enabled to establish educational departments and the needed personnel in each of the military hospitals where the work was required. Each hospital was supplied with a chief educational administrative officer, commissioned officers qualified as general and special educators and psychologists and noncommissioned and enlisted men able to serve as teachers and instructors of patients in the application of curative work in the program of physical reconstruction.

The director of physiotherapy in the office was able to secure a sufficient number of qualified medical officers to serve as directors of the work and a personnel of other commissioned officers, noncommissioned and enlisted men and trained qualified women aides in physiotherapy efficiently to apply physical treatment to disabled men.

Recreation in the form of exercise in gymnasiums and out of door games was secured through the American Red Cross cooperating with the Y. M. C. A., the Knights of Columbus, the Jewish Welfare Board and in the base hospitals and convalescent centers through the War Department Training Camp Activities.

WARD WORK

In the application of the curative workshop schedule, work in the wards for bed and chair patients was applied by women as reconstruction aides in occupational therapy. These women were qualified for the work by experience as teachers in high schools, colleges and universities in civil life and by special training in arts and crafts. Some of them had served in civil life as social welfare workers.

The ward work has proved of the greatest value in the cure of patients. Primarily, application of the work served as a diversion by arousing the interest of the patient and by distracting him from a contemplation of his disabled condition, whether due to sickness or to injury. At the beginning the schedule of ward work consisted of simple handicrafts in the form of knitting, beadwork, basketry, mat-weaving, block stamping, wood-carving and the like. As the work progressed, it was found that the interest of the patient was more readily aroused by work that was prevocational or even vocational in character, because it prepared him for the occupation that he would follow after discharge from the army or for further education and training by the Federal Board of Vocational Education. Consequently stenography, typewriting, mechanical drawing, winding electrical armatures, academic and commercial study and the more purposeful handicrafts were utilized.

As rapidly as possible buildings were altered or new ones constructed for workshops and schools, equipment installed, books were obtained through the American Library Association, and the convalescent patients were sent to the shops and schools for the application of the doses of work prescribed by the ward surgeons.

SHOP WORK

The schedule of work in the shops consists of motor mechanics, boot and shoe repairing, harness making, carpentry, electrical installation, printing, mechanical drafting and the like. In the gardens, landscaping and truck gardening are taught; on farms, ordinary farming, including stock breeding, dairying, poultry raising, hog raising and farm economics. Greenhouses are utilized at many centers to train men in horticulture and to grow vegetables. In the schools academic studies in common school branches including left hand writing are taught. Incidently, aliens, and especially the illiterates, are educated and then naturalized as American citizens. Commercial courses are given in shorthand, typewriting, bookkeeping, banking, buying and selling, and many other branches.

At the U. S. General Hospital No. 11, Cape May, an efficient school for the disabled soldiers with deafness and defective speech successfully teaches lip reading and the correction of speech defect. The patients coincidently receive prevocational or vocational training.

CARE OF THE BLIND

At the U. S. General Hospital No. 7, Roland Park, Baltimore, there has been established a school for the blind or nearly blind soldiers, sailors and marines. The blinded soldier is taught how to dress, feed himself and get about as an independent person, at the same time thorough instruction is given in Braille and coincident training in occupations suitable for the blind. In this connection, there are approximately one hundred totally blind, and approximately one hundred partially blind soldiers, sailors and marines.

THE TUBERCULOUS

The schedule of curative work applied to the disabled soldier suffering with pulmonary tuberculosis was modified to meet the varying clinical conditions under constant watchful medical supervision. Curative work for the tuberculous soldier has proved of the greatest value in the prevention of hospitalization and for the convalescent in the production of the final hardening process so valuable in the prevention of relapse, when the stage of inactivity of the disease has been secured.

SPECIAL CENTERS

A few of the general hospitals have been designated as special centers for the treatment of the nerve injuries, the maxillofacial mutilations, and of the amputation cases. At two or three centers, provisional artificial limbs and protheses are manufactured. There the men with amputations are fitted and trained in the use of the artificial appliances. In this connection it should be stated that the Bureau of War Risk Insurance is responsible for furnishing the discharged soldier with the needed permanent artificial limb.

COOPERATION

In the application of curative work in the treatment of disabled soldiers it has been the endeavor to secure cooperation between the ward surgeons and the educational department. It has been recognized that the justification of the adoption of work as a therapeutic agent involves control by the surgeon and physician; that while the educational officer may evolve kinds of work, which to accomplish the end sought requires known muscular action, it is the surgeon or physician who must indicate the particular function to be restored and to prescribe the dose of work, the time it is to be given and the frequency of its repetition. The same cooperation is necessary between the clinical staff and the director and his personnel in the application of physiotherapy.

"CHEER UP" PROPAGANDA

For the information of the disabled soldier circulars and bulletins have been published by the Medical Department of the Army outlining the program of physical reconstruction in the military hospitals. "Cheer up" propaganda has been placed in the hands of the patients and for their benefit, and, to educate the general public on the need of physical and functional rehabilitation, the Surgeon-General has published and distributed, with the cooperation of the American Red Cross, a magazine "Carry On."

Cooperating with the Federal Board for Vocational Education, the Surgeon-General has compiled and published courses of study in pamphlet form, covering all phases of study and occupations as guides to teachers and patients, in the application of the curative workshop schedule in the wards, shops, schools, gardens and fields.

To the date of the signing of the armistice the educational activities applied in the treatment of the disabled soldier justified the vocational training of the convalescent soldier to fit him for further special military service. Until that date the general hospitals which functioned in the physical reconstruction of disabled men returned many men to general or special military service, and of these, the majority had been sent to the hospitals, with the belief they could not be made fit for further military duty. The application of curative work, physiotherapy, military drill, special training and play were the decisive factors in securing such complete physical and functional restoration that they were able to return to military duty.

THE RETURNED DISABLED SOLDIER

Following the signing of the armistice and the cessation of hostilities it was no longer necessary to keep the disabled man in overseas hospital until restored, because he would no longer be needed for military service unless he had enlisted prior to April 6, 1917. Consequently, it became necessary to amplify the centers in this country for the physical reconstruction of the large number of disabled men from overseas who returned to America for treatment. To meet this need facilities were provided by the War Department at the request of the Medical Department, for physical reconstruction of disabled soldiers in departmental base hospitals and in base hospitals of the National Army cantonments. Additional general hospitals were also equipped for the work until a total of 40 hospitals were designated to function in the physical reconstruction of disabled men. In addition to the hospitals, 19 convalescent centers were established in the training camps of the country to which convalescent detachments from overseas and convalescent patients from the hospitals of this country were distributed, each one sent to the center nearest his home, for a final process of hardening by the application of curative work both manual and mental, by general and special physical training through military drill and calisthenics, and by exercise at play in gymnasia and out of doors.

Since the armistice was signed the policy of the Medical Department of the Army is to discharge the disabled man as soon as he shall have reached the maximum physical and functional restoration, consistent with the nature of the disability. This leaves to the Federal

Board for Vocational Education the responsibility for the occupational training and education which is the privilege of the compensable disabled soldier if he desire to take it. The application of physical reconstruction or ,a better term, physical and mental rehabilitation of disabled soldiers, has been justified by the result in the military hospitals of this country. With a small beginning it has grown within a year of practical application to a large establishment.

PERSONNEL

The personnel of educational officers with their subordinates, non-commissioned officers, enlisted men, as qualified administrators and instructors are as fine a body of men as one will find anywhere. They have given patriotic and efficient service to the country and have been and are recognized factors in the more complete physical and functional restoration of disabled men, who have thus been made fit to return to their old or a new occupation or have been physically and mentally prepared to take advantage of the opportunity for vocational training and education under the authority of the Federal Board.

Approximately 800 reconstruction aides in physiotherapy have given efficient service in the application of local baths, electrotherapy, massage and passive exercise to disabled men at home and overseas.

Approximately 1,400 reconstruction aides in occupational therapy have rendered service of the highest efficiency in the application of mental and manual work for the patients in wards in overseas and in domestic hospitals. These women who have served the government as reconstruction aides in physiotherapy and in occupational therapy are deserving of the highest praise for the work they have done for the disabled men.

It is common expression of all officers who have come in contact with the disabled sick and wounded soldiers that the application of curative work and physiotherapy has done much to improve the morale, maintain discipline, prevent hospitalization and to hasten and make more certain the cure of the patients.

PERMANENT POLICY

It is believed that the experience and application of curative work and standardized physiotherapy in the military hospitals during the emergency created by the war, will become a permanent policy of the

military establishment of the United States. This policy will necessitate the designation of certain general and military post hospitals to function in the physical reconstruction of the sick, injured and disabled men. Facilities for this work in military hospitals will include the application of curative work that is vocational in character. Vocational training in the military hospital is justified by law and by the fact that the disabled soldier may continue in military service provided the nature of the disability permits restoration consistent with further service. The vocational training and education received while a patient will make him of greater value as a soldier and at the expiration of his term of enlistment, should he decide to return to civil life, he will serve with greater efficiency in the industrial army.

II. REHABILITATION OF THE DISABLED OF THE INDUSTRIAL ARMY

It has been stated that 750,000 people of 18 of the United States of America are injured annually in the industrial occupations. Of these, 35,000 are permanently disabled. It has also been stated that 80,000 people are permanently disabled annually in the whole United States through accident received in industrial occupations. Of these it is stated that 2,000 are totally disabled.

This enormous crippling or entire loss annually of the industrial workers has not received the consideration due these unfortunates by federal, state or local governments, or by corporations engaged in industrial work.

Sporadic attempts have been made by local communities or by corporations to overcome the handicap due to the disability by the application of measures of physical and mental rehabilitation. But, as stated, the attempts have been purely local, small in character as compared with the enormous problem and have been characterized by partial success only because of the lack of uniform standardization and application of the work.

The application of mental and physical rehabilitation to sick and disabled soldiers by practically all of the nations engaged in the war has proved so successful and beneficial that it imperatively demands the application of like measures for the benefit of the disabled of the army of the industrial world.

The need of the physical and mental rehabilitation of the disabled of the industrial army of the United States has already received the

earnest consideration of thoughtful members of the United States Congress, of Federal Department officers, of governors and other officers of some of the states, of the heads of great industrial corporations, of members of the medical profession, and of the workers themselves.

The success of the mental and physical rehabilitation of disabled soldiers under the administration of governmental authorities cooperating with civilian organizations in England, France, Italy, Canada and other countries, and under the War Department of our own government cooperating with the Bureau of War Risk Insurance and the Federal Board for Vocational Education, suggests a similar initiation of the mental and physical rehabilitation of the disabled of the industrial army.

FEDERAL ATTENTION TO THIS PROBLEM

In this connection it is suggested that the mental and physical rehabilitation of the disabled in civil life should be standardized by federal law. Federal responsibility in the welfare of the people of the country should be a reason for the enactment of federal and state legislation which will establish the compulsory application of measures of prevention of disease and injury and rehabilitation to overcome the handicap of those who, in spite of the application of precautionary measures, are disabled by illness and injury. The responsibility for the efficient and practical application of physical and functional rehabilitation of the disabled should lie with the state, the muncipality or other local communities. The cost of the rehabilitation of the disabled should be borne in proper ratio by the federal, state, county and municipal governments and the corporations employing labor.

MILITARY EXAMINATIONS SHOW NUMBER OF UNFIT

The problem of mental and physical rehabilitation of the civilian population disabled by illness and injury involves primarily the application of known scientific and other practical measures of disease and accident prevention. It is significant of the need of the application of known practical and efficient measures of disease prevention that approximately 50,000 registrants were rejected because of pulmonary tuberculosis by the local draft boards and the military medical examining boards of the training camps. Many of these young men were

unaware that they suffered from the disease. The draft boards and the training camp officers detected and rejected as unfit for military service approximately 53,000 registrants made defective by acquired or congenital nervous disease or mental deficiency. Other disqualifying conditions due to preventable diseases caused the rejection by draft boards of thousands of our young men.

DISEASE AND INJURY PREVENTION

The experience resulting from the war emphasizes the need recognized for years by sanitarians and many physicians of the compulsory application of measures of prevention of infectious and other acquired and congenital diseases or morbid conditions. Well known and safe means of immunization will practically banish smallpox, typhoid and paratyphoid fevers. The efficient application of the laws of sanitation will abolish or diminish to a negligible degree malaria, hookworm disease, cholera, bubonic plague, tuberculosis, trachoma, dysentery and other diarrheal diseases which are so productive of temporary or permanent disability. Venereal disease prevention should be enforced by measures which command known medical knowledge and skill reinforced by the police powers of the state. Fortunately, alcoholic misuse and the harmful results to the individual and through him of others, will soon cease to be a national menace. Marriage and birth control are essential measures of prevention of an increasing number of the physically and mentally unfit. Many of these unfortunates are dependent from birth on society for their maintenance or become so because of nonresistance to disease or because they are physically or mentally unable to safeguard themselves from industrial or other injury. Individual hygiene and the prompt treatment of trival injuries and illnesses and the thorough eradication of foci of infection will usually prevent more serious consequences.

The war has shown us the value of a life in the open with regular hours, directed exercise, a simple dietary and the use of sensible shoes, as measures for developing resistance to disease and the maintenance of healthful vigor. Many industrial corporations have already learned the value of the application of measures of disease and injury prevention. Better sanitary conditions have been established and safety devices adopted which have been of the greatest value to employer and employee. These measures of safety provision should be standardized and universally applied, under a law of compulsion.

USE OF CIVILIAN HOSPITALS

Rehabilitation of the disabled in civil life should begin in the civilian hospitals just as it has received its primary application to the disabled soldiers in the military hospitals. There is this difference, however; the military hospital is justified in the application of curative work having a vocational trend which will make the soldier of greater value to the army when he shall have recovered.

In the civilian hospital the application of curative work in the treatment of the patients is justified as a curative measure which makes more certain and more rapid the recovery of the patient. Every civilian hospital which serves a large community should maintain a department of physiotherapy properly equipped in which standardized and efficient physical treatment may be given to the sick and disabled who require it. But a civilian hospital cannot become or be maintained as a vocational school or college in the sense of educating and training the sick to better qualify them for an old occupation or to train them for a new one.

The function of the hospital in the treatment of the sick ceases when the patient has reached the degree of maximum physical and functional restoration. If the patient is permanently disabled by sickness or injury and the handicap due to the permanent disability needs to be overcome by vocational training and education, the convalescent patient should receive this elsewhere than at the hospital.

INDUSTRIAL TRAINING SCHOOL

It is my belief that the time has come when industrial training centers with properly equipped shops and schools must be maintained in every great manufacturing and industrial center where the disabled, both temporary and permanent, but especially the latter, may receive the training and education necessary to qualify them to continue in the old jobs or if necessary, to qualify them for new occupations. By cooperation with existing industrial shops and schools this training and education may be carried on without great expense. The opportunities offered should be made available for the convalescent disabled men and women discharged from all hospitals of the community.

This project should receive the financial and moral support of the responsible business heads of the great railroads, great manufacturing

interests, public utilities, and all persons able to aid who are interested in the welfare of their fellow men. It should receive the enthusiastic support and cooperation of all industrial workers.

PENSIONING OF THE DISABLED

Government pensions for permanently disabled soldiers and compensation for industrial accidents are just measures of relief. This money compensation never adequately compensates the injured individual for the disability suffered. The compensation does afford him means which should encourage him to take training necessary to rehabilitate him and to fully overcome the handicap due to the disability.

CONCLUSION

The government maintains homes for the disabled soldiers. Counties and municipalities maintain hospitals for the free treatment of the poor and almshouses for those no longer able to maintain themselves because of physical disabilities due to serious injury and old age. These homes for dependents are also justified by the need, but if proper measures are applied adequately to rehabilitate, by proper training and education, those disabled by sickness and injury, the large number of dependents of the military and industrial armies, who have in the past and may continue in the future to suffer the prolongation of a relatively useless and unhappy existence in these institutions, will be greatly decreased, if the measures advocated herein are carried out.

THE MENTALITY OF CONVALESCENCE

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May 1, 1919

I appreciate deeply the honor done me as a layman in this invitation to address you. May I suggest that, having in mind the whole panorama of military medical achievement, we consider for a time the mental attitude of the patients concerned, particularly of cases involving the restoration of function. To present this topic in the form of two questions: First, Is a patient's conscious reaction to his condition and treatment a matter of any consequence as a general rule? Assuming for the time being that the patient's attitude is not just what the practitioner would desire may we enquire, secondly, How should this psychological factor be handled? May it for instance, be ignored or be passed over with a casual word of counsel and encouragement, or should a scientific procedure be adopted throughout, i. e., accept that mental attitudes, like other symptoms, show great variety and change, that characteristic attitudes result from definite antecedents, that they exhibit certain uniformities in developing, sometimes pass through crises, and regularly respond to certain lines of discriminative treatment, etc.?

The undefined term, mental attitude, is not here used as synonymous with any of the "psychical effects" often alleged to be produced on patients by this or that apparatus or drug with which they are deeply impressed. Such phenomena, half-mystically accepted by some practitioners, though without any critical or reasoned view of the underlying principles involved, may or may not be a factor in a patient's general attitude. Nor is the term intended as peculiar to those purely hysterical disorders of the war, which, perhaps happily, have compelled attention to psycho-technics that were formerly practiced only by leading neurologists and psychiatrists. Again the term is in no way restricted to that difficult group of cases showing a mixture of physical and "functional" involvement that has demanded the team-play of specialists. A broader use than these is intended, viz., that state of

mind which, however complex in itself, is characteristic as marking a great gulf between the invalid and the well man, whatever be the lesion or pathological condition.

An appreciation of the mentality of convalescence means in the first place recognition of the fact that treatment for the restoration of function requires more than plaster casts and braces, lances and ether, baths and massage benches, etc., however skilfully these be employed. The condition in large measure concerns voluntary functions which, having once been part of the patient's normal equipment for the activities of daily life, are now absent or seriously impaired, with the result that his life has shrunk to a degree that can accommodate that loss. To restore crippled functions requires the physiological and mechanical basis, but likewise effort, insight and perseverance by the patient. Formerly these functions operated with ease, now the habit of inaction or of substitution is ingrained and stabilizes a "set" of maladjustment. To overcome the latter is a course of high resistance that is neither natural nor congenial. For this reason a purely impersonal technic is not adequate. The very depths of a man's nature must frequently be reached and stirred in order that he play his part, for without desire and determination we look in vain for effective action. The motives which are fruitful are as various as human nature is complex, and the selection and application of them cannot well be left to a chance environment. Treatment must be fitted to the man as well as to his ailment. The opposite point of view might be illustrated by a type of political economist who in his endeavor to analyze rents, wages, prices, etc., sees not the folks whose deepest instincts give such concepts life. Is the therapeutist safe from the same pitfall until he sees a patient as more than bone and blood? Crude though the family physician's psychology may be, it has a power which specialized medicine can profitably develop and refine. Now, when modern medicine is aiming to carry its benefits of prevention and cure into the realm of organized industry, the time seems fully ripe to stress this point of view in medical education and practice.

This is not the occasion to present a detailed analysis of the mental attitudes of either military or industrial patients even were I competent to do so. A few points and illustrations rather arbitrarily selected may serve to indicate certain problems and remedies which our military experience has suggested.

The setting for diagnosis of a veteran's point of view is important. One's mental outlook is not merely a personal possession, but a sensitive living organism with a life history and unlimited potentialities. It may be guided more frequently than driven. The object of an interviewer is not so much to gain knowledge as to leave an impression and if possible an inspiration. Interviews should, therefore, be individual and characterized by brevity, frankness, confidence and a sympathetic understanding conveyed by tone and manner rather than by words. Labored questioning on civilian history and service record serve usually only to confuse, chiefly because the man is accustomed to be paraded and give his report or receive instructions. Facts which his papers would reveal at a glance need not be rehearsed; it is more impressive for the interviewer to show the possession of such knowledge than to elicit it. Man to man contact, eye speaking to eye, has in it a power which should not be distracted by the filling in of forms. From this standpoint the initial interview is a first and invaluable step in treatment. With the constructive phase of the interview we shall deal later. Our present point is the importance of what may be described as the unspoken communication. This does not imply pauses of silence, but it does mean the exercise of a fertile and appreciative imagination which reads the background of the patient's past accurately. This fact is impressed upon the patient by the nature of the program outlined for him.

In the training of civilian workers for functional reeducation we have been impressed by the advantages of dwelling on certain features of the veteran's mental outlook. That the veteran is different from the civilian is immediately recognized, but failure to understand how and why is disconcerting and invites indulgence in sentimentality. On the other hand, to give students a critical curiosity about this side of the case stimulates close observation, assists in adjustment to the needs of the individual and adds immeasurably to the interest in the work.

This pedagogy must pierce below generalities to a study of individuals. The attitude of a patient depends not merely on what he was before enlistment, but on what branch or branches of the service he has been in and the conditions and length of his service and hospital experience. The outlook of an infantryman differs from that of an aviator, as a counter-battery artilleryman's does from that of a naval cadet off a submarine chaser. A patient's attitude is not simply a

product of his hurt or of his hospital environment, but of his whole service. It is habits of thought that make problems of re-adjustment, and for this reason the ultimate cause of "hospitalization" should be sought not in hospitals, but in certain unavoidable features of combatant service. This may be illustrated in an abstract way from the experience of the healthy infantry recruit.

Whether he be a draftee or a volunteer, his first job is to learn to be a soldier. To say that this means he loses his individuality and initiative is less accurate than that it means a narrowing down of the motives upon which he may act. "How little," writes a soldier from France, "the outside world understands what our lives are like. In the outside world there are standards of freedom and politeness; in all personal matters a man has the power of choice. He is at liberty to make or ruin himself. He washes if he so desires; if he prefers to go dirty he does not wash. Within reason, as far as is compatible with the earning of his daily bread, he sleeps as long as he wants. . . . With us everything is reversed. We grow mustaches under Army orders, we crop our hair to please the Colonel. We have no areas of privacy either in our bodies or our souls. We rise, sleep, eat, wash when we are commanded. We are physically examined, physicked, pumped full of antitoxins and marched off to church parade to worship God without our wishes being consulted. . . . We cannot give notice to our employers, we have no unions, no means of protest. To be always cheerful and smiling, the more cheerful and smiling in proportion to the hardship is a duty for the performance of which we expect no thanks. . . ."

Success in civilian life demands foresight, judgment, decisions that involve responsibility. All this must shrink to the vanishing point. In the ranks I do as I'm told. I do not think what I am to do, but I must think what I am doing. I am not a good soldier until my critical instincts are inhibited at least to the extent that they do not feel outraged nor plead for indulgence because of the limitations of my rôle. Nevertheless, room for initiative remains in the giving of prompt and accurate obedience, neither understepping nor overstepping the mark, expecting neither gain nor glory. Precision requires concentration and restraint, and for reward I may cultivate such chronic good humor as I will. This contraction in motives is a moulding process that requires time and adaptation. It is more disagreeable in the learn-

ing than when accomplished, but the unlearning seems most difficult of all.

With the narrowing of motives necessarily come changes in values, some more significant than others.

The personal equation must be adjusted. In civilian life we each adopt a particular point of view to all whom we meet: our banker, our grocer boy, our member of parliament, our doctor, our aunts, the stranger we pass. We carefully classify and appraise our social environment for what it means to us, and our daily routine becomes a dove-tailing of reactions appropriate to the great variety of our associates. On enlistment this grading of associates is ironed out. We each have our number, we think together, act together, play together, we belong to the dead level of Tommies. Beyond this are no distinctions of person, only of rank, which is for the most part a philosophy of clothes and an appreciation of idiosyncrasies.

The limiting of responsibility has far-reaching effects. In ordinary life our tasks rarely stand isolated, they blend with one another and with the activities of our fellows. Under such circumstances the attainment of results is more significant than the detail of the means employed; in other words, experience counts, discretion is expected, economy in time and effort is approved. In the army tasks are sharply focussed. To concern oneself with more is to be guilty of an offense. Instructions mark the limit both of responsibility and of power. Time means nothing. Ultimate results are not your concern. Explicit obedience to superiors to the last detail is at once your duty and salvation. This limitation of responsibility the soldier learns too well, he even achieves skill in shifting to others the small responsibility he has. The fruits of this planting ripen during convalescence. His active duty has then ceased, but his attitude of dependence remains and is seen in his cheerful resignation to passivity. He is overwilling to be managed from without, not from within, even in the matter of improving his condition.

Many of the major moral forces and behavioristic reactions which serve to stabilize society are inhibited or reversed in active service. Habits that make for conservation of life and have been a life-time in building are changed into a will to risk or take life. Discipline and common sense are not always sufficiently powerful substitutes for the sanctions of the home, the church or the club. The horrible sights

and acts, the verminous nights, the moments of controllable emotion, of fear, disgust or passion, the swift partings, such things which deeply burn, we who have not been there can know nothing about even though our pulse may quicken over some bit of realistic verse from the trenches. The oscillation between extremes, for example, between periods of work of heart-breaking severity and rest periods of comparative idleness is probably more of a tax on stamina than the deadliest monotony of industry can ever be. It is not during action but in billets after action that hysteria usually incubates. Too great contrasts inhibit control. The degree to which such experiences reduce the power of re-adaptation to the civilian outlook is in some cases probably considerable, though always difficult to gauge.

True to the laws of life and growth the human mind accommodates itself to a change in mental environment. Characteristics which formerly were important tend to disappear and others are acquired. If the change is rapid and extreme in kind as on entering military service the adjustment is more marked. It is the new "compensation" factors that become dominant. They form the retaining walls in a new level of mental equilibrium; they are the foundations of successful training and of high morale so long as the environment of active service continues. Should a different setting arise as during convalescence or at discharge or, more generally, when the armistice was signed, the equilibrium is again disturbed. If, for instance, it be a question of re-entering civilian life the problem of adaptation is two-fold, viz., the reinstating of discarded motives and the reduction of those which have sustained him through the hardships of service. The relearning is here easier than the unlearning because the latter motives are founded on the most primtive and strongest instincts in man.

Perhaps the most dominant compensation factors in military life are those instincts which make possible and stable a gregarious male existence. One has but to reflect on the satisfaction with which we seek the seclusion of our home or club after but a few hours in the company of our business associates to realize what adjustments would be required for us to live congenially elbow to elbow for months on end with men not of our own choosing. These adjustments are both discriminative and assimilative. A man who is not in harmony with the group has to be discriminated against as a menace. He is ostracized in countless ways by his fellows. If the satirical remark or practical

joke are not sufficient, plain words or forcible action must follow. What in ordinary society might be a harmless eccentricity becomes an intolerable nuisance or danger in gregarious life. The herd cannot escape from the offender, it must, therefore, cure him. This is the negative or protective phase of adjustment.

The positive or assimilative phase of the gregarious instinct is that comradeship of companions in arms which is as old as war. It is not based to any large degree on the luxuries or pleasant things of life, on any similarity of tastes or hobbies. It is not a partnership, there being rarely anything to apportion. Its external side is simply a common inheritance of hard marches, wet trenches, good grouches and, withal, cheery smiles. Fundamentally, this comradeship rests on the feelings and aspirations of a whole body of men who have a common and hard lot, and who know that while they may fall before it one by one they cannot rise above it except together. The feeling is not one of liking the task, the aspiration is only to see it through. Every good officer knows that this factor is a cornerstone in the structure of esprit de corps. With this feeling strong within him no man can hold back when his comrades go forward. Nevertheless, though this comradeship has been vital to the Army, helping the men stand shoulder to shoulder in the trenches, its usefulness is not so evident on return to a civilian setting if it tempts men to sit side by side on our park benches when work is to be had. To modify a strong instinct on which one's existence has long depended is surely as difficult as to master a trade. The quality of human nature which produces the companionship of the trenches likewise produces veterans' associations and trade unions; it may be guided, it cannot be repressed.

Two instincts of expression which gregarious army life fosters and is for are fighting and playing. The one is an unpleasant necessity, the other a pleasurable substitute or equivalent. That the play instinct, as expressed in physical sport, seems spontaneous in our Army is suggestive of a fruitful means of stimulating physical action in crippled men whose fighting days are over. There is also a current of playful humor that flows near the surface in the Army. It may be shallow, because a herd is never intellectual, but it is expressive, and is one of the ways of relieving the feelings and of passing the time congenially. In this connection we should not fail to appreciate the extent to which poker and crap helped win the war.

We have referred to some factors in the soldier's mentality, whether he was physically incapacitated or not, which must be reckoned with in rehabilitation. May we now consider certain influences these produce in the outlook of the wounded man and then formulate the problems and remedies for the peculiar mentality of military convalescence.

Until the soldier falls out his existence as an individual is nil, then all of a sudden he becomes important. He is no longer told what to do, he receives attendance, others act for him. His companions have gone forward, he goes back. No longer has he to keep pace with anyone, he is out of the race. This is a complete change of setting and produces a corresponding mental reaction. Realization of his "blighty" is the occasion of profound relief that knows neither reservation nor misgiving. The positive forces fall away without compensation. Unlike the civilian casuality who feels the distressing responsibility of provision for his family and himself, the soldier is aware that provision is assured. He calmly waits for what the future may bring forth.

The initial and most significant point in his mental adjustment is this unresisted slump in his "reaction of effective capacity." Whether his hurt be grave or slight, there is now no appeal for action either from without or within. From a circumstance wherein he strained every nerve to fall not short, he has fallen suddenly to a level where no goal exists. This slump in will is, of course, not peculiar to the war casuality, it may be seen on every hand in civilian life, in the school child who loses his place through unavoidable absence, in the laborer who loses first his place then his inclination to find another. But in the soldier, owing to his mental antecedents, the slump is more striking and the restoration of positive values more difficult. A new outlook has to be created, perhaps in the face of the fact that it was not a healthy thing to get well before the armistice. To restore his keenness, to find a motive appropriate to his state of mind is then the immediate problem of reconstruction.

The soldier's habit of not assuming but avoiding responsibility inculcated in his days of service finds full indulgence during convalescence. He takes his treatment with philosophic complacency. He is more satisfied to be worked at than to help himself. The remedy again lies in altering the point of view.

The convalescent Tommy is surely the most impressionable of men. Since enlistment his sphere of action has been narrow, with little variety or complexity. Situations which formerly he would have carefully weighed he now interprets only with himself as center. Not understanding the mysteries of medicine he has more than the usual reverence for the opinions of his medical advisor. The latter, being usually at pains not to enlighten him, leaves his uncritical imagination free rein. A doctor's prestige rests partly on a patient's vague alarms, and the fears of the military patient incline toward pessimism. He interprets the most casual and even irrelevent remarks as pertinent to his own case. He regularly selects only the unfavorable indications and the resulting picture is gloomy indeed. If he quotes you an earlier prognosis it is one that harmonizes with his present view and is usually attributed to an officer of wide reputation who is at least two ranks higher than yourself. Such an attitude is not morbid, but a natural outcome of his service experience; it is an attempt to rationalize his passive conduct. The remedy must be through motives that are sufficiently powerful to appeal.

Though the soldier's pessimism is self-centered, he does not keep it to himself. The gregarious habits of active service are a suitable soil for the growth and spread of his deepest feelings. Unless careful counter measures are applied a depressing atmosphere of convalescence becomes the prevailing tone of the hospital. The patient sees little to hope for and applies frequently for leave or even for discharge.

When a patient does show interest about his own improvement not infrequently it is a misplaced interest. He shows a keen belief and confidence in some irrelevant apparatus or technic which is not available, and at the same time he is not inclined to be a partner in what is being done for him. If he is being treated with a galvanic battery he feels that a certain violet-ray machine which he once saw is what is required, Or, if his amputated stump is weak from want of graduated exercise so that he cannot operate his artificial arm, he complains that the latter is useless. He knows, too, of a high priced American arm that is satisfactory, the Canadian government cannot make proper arms anyway, he hands in an application for leave and intends to cross the line and buy one.

The mental mechanism in this attitude is neither morbid nor unnatural. We tend to ignore, to put away and forget what is highly

unpleasant. For him the unpleasant is the manifest disability which stands between him and comparative health. He does not face the facts. In turning aside from his crippled function he ignores or belittles the measures which might bring relief. Instead he pins his faith to something which is just over the horizon or always falls short of being of any practical use to him. This becomes an imaginative construction which he amplifies and garnishes to his liking, and in proportion as his false ideal grows so does his inclination to help himself in any practical way decline. A danger therefore in any program of treatment based on the principle of helping a patient forget his disability is that it aggravate this inclination toward self-deception and the way of least resistance which is already a chief difficulty that he has to combat.

Such factors as the above, the slump in desire for accomplishment, the resignation to circumstances by the individual and the group, the rationalization against self-help, and the forgetting of the real issue in lieu of a false one — these may serve to indicate our problem. Not all of them appear in every case or in like degrees and the attitude varies as the physical condition changes, but observation of one thousand cases has satisfied me that they play an important rôle.

In referring to principles of treatment as relative to the mentality of convalescence it is assumed that the medical, surgical and passive therapeutic needs are being attended to, and that active functionating preliminary to more complete rehabilitation is required. The program should be fitted to the patient's point of view as well as to his physical condition. "The invalid," says Prof. E. J. Swift in his Psychology and the Day's Work, "who waits till he feels able to work will never begin." The same may be said of the beginnings of functional restoration. Let us accept further that the test of effective procedure is twofold. First to reduce his disability of useful function to a minimum in the least time, the claim for as quick results as medical safety permits, being not merely economic but because success is the best stimulant to a patient's effort. Secondly, and so far as possible simultaneously, to restore his self-confidence to the maximum and to direct and fit him to an objective in civilian life.

The value of curative occupation is now widely recognized on both sides of the ocean. It is properly argued that, man being a manufacturing animal, from the day our patient owned his first jack-

knife, and even earlier, he has been making things. Therefore develop the motives of making with the infinite wealth of originality that that field opens. Interest the patient in things, jobs, objective results. Let his hands be occupied and his mind will be taken off himself. To those who are following military work the validity and results of this principle need no argument.

But human nature is very complex and may be approached from various angles. Visible products of his hands are not the only things that stir in man the conviction of accomplishment. If it is instinctive to mould clay into marbles, it is just as instinctive to play marbles — and more energetic. The motives of *doing* like those of *making* have unlimited possiblities of appeal. The problem in convalescence being to overcome apathy and establish desire, it is not so much what he does as the source of his effort that matters. In this sense the merit of a method is its fitness to touch the springs of action. It is because the motives of individual expression have been repressed and those of group effort have been made dominant in the service that through the latter curative action may be readily stimulated.

In this way it is possible to approach the patient's disability and attitude directly and present a constructive program of applied exercise. In the initial examination and interview, pains are taken to have him see the exact deficiency of function in range and in strength as compared with the normal. The problem that stands between him and health is then squarely before him. Challenge him to undertake the task and you arouse his fighting spirit. He volunteers. He is told that he will be shown what to do and how to do it, but that he must do the work. It is impressed on him that his object is to improve his condition, and he is warned that he will get out of the treatment just what he puts into it, nothing more, and that you are going to watch his progress. Few patients indeed fail to respond with their heartiest cooperation. Should this occur the reason lies still in the mental attitude and must be sought out and met. Re-examination and systematic supervision are as important as the initial interview in cultivating the proper attitude.

A complementary side of this direct treatment lies in the proper equipment and trained personnel to administer graduated exercises suited to various disabilities. With the details of these methods, the progression through muscle function training, higher co-ordination

and collective gymnastic work we need not be concerned. Suffice it to say that the aim throughout is to combat the attitude of invalidism by setting precise tasks, not minimizing difficulties, and appealing to the strong motives of mastery, of self-competition and group competition. The results have been most gratifying.

To sum up the principle of the direct method as a remedy for the mentality of convalescence. For each negative element of the latter is substituted a positive one based on powerful emotions which the veteran knows. Instead of allowing the patient to relinquish responsibility he is forced to assume it by having him measure up to expectation in working out his own salvation day by day. His extreme suggestibility is taken advantage of to impress a constructive program stimulated by the instincts of sport and competition. His false idealism which would forget the facts and look for relief to something outside or beyond reach is banished by converting him to an enthusiastic use of practical means at hand. Lastly, his strong gregarious habits are utilized to cultivate an atmosphere of cure rather than of convalescence. Establish the conviction of improvement in individuals and it will spread through a whole patient population, then collective treatment may complete the process.

The time has probably not yet come to draw final conclusions regarding the relative psychological efficacy of different methods of treatment during convalescence. Though the war experience has been large, the opportunities of careful comparison of distinct methods, conducted to the same end and under similar circumstances have been few. One's opinions consequently reflect chiefly one's own practice. It might be objected, for instance, that in the direct method of functional restoration men are asked to concentrate on insignificant and unmannish tasks, and that these will only emphasize the disability in their own eyes. But the criticism reflects the standpoint of the well civilian rather than the military convalescent. In the struggle for improvement small things to him loom mountain large, and that which impresses him is what he does accomplish rather than what he does not. On the other hand, the direct method, being intensive, should be tempered by occupation and objective tasks.

Among the problems of the future therefore will be the proper balancing and interrelating of technics that will be most appropriate to convalescence in the widest sense. The mental attitude of patients

in war service is complex, but is immeasurably simpler than the points of view met outside the service where patients of both sexes and all ages await similar assistance. To find the facts about the attitude of workers in industry, for instance, is a vital task today that is little more than commenced. If medicine, therefore, sees new service in the field of industry ought not the psychological factor to have a place in its program and an influence on its therapeutic procedures?

DIPHTHERIA IN CHICAGO

Report of Committee on Local Public Health Problems, Institute of Medicine of Chicago

The committee considers that the present status of diphtheria in Chicago is such as to invite special attention on the part of the Institute. The following table shows that for a number of years past diphtheria has not only been higher in Chicago than in other cities in the Middle West, but that it has been higher than in any other city in the country with over 500,000 population.

TABLE 1

Diphtheria Death-Rates per 100,000

	Average 1910-1914	Average 1915-1917
Chicago	38.2	35.6
New York	27.6	20.7
Boston	20.0	29.9
Philadelphia	23.8	22.3
St. Louis	23.8	24.2
Cleveland	26.5	21.7
Baltimore	13.8	11.1
Pittsburgh	28.9	23.3
Milwaukee	29.8	20.7
Minneapolis	27.9	18.3
St. Paul	31.0	12.3

It is true, moreover, that while all the other cities in the list showed a lower diphtheria rate in 1915-1917 than in 1900-1904, Chicago had a somewhat higher rate (1900-1904 = 33.9; 1915-1917 = 35.6).

According to the published reports of the U. S. Public Health Service, the indicated fatality rate per 100 cases of diphtheria has been higher in Chicago from 1913-1917 than in any other large city except Philadelphia.

TABLE 2.

Indicated Diphtheria Fatality Rate per 100 Cases

	1913	1914	1915	1916	1917
Baltimore	6.19	7.38	6.86	8.31	8.41
Boston	7.08	6.32	7.49	7.68	6.73
Chicago	11.28	10.86	11.60	11.26	11.82
Cleveland	8.02	6.77	8.03	6.29	8.35
Detroit	10.15	7.73	6.11	7.16	9.14
Los Angeles	7.82	5.05	5.15	5.00	5.87
New York	9.17	8.70	8.36	7.63	9.17
Philadelphia	13.76	12.41	12.05	15.33	14.17
Pittsburgh	12.35	9.67	10.23	9.77	9.36
St. Louis	7.41	6.95	5.04	5.45	5.45

Compiled from U. S. Public Health Reports.

Since diphtheria is to a large extent a preventable and curable disease, the relatively high death rate, the high fatality rate and the absence of and material improvement in Chicago during a period of 18 years seem to call for increased publicity.

As is well known, the reduction of diphtheria morbidity and mortality is largely a matter of administration and education.

The evident measures for reducing diphtheria in Chicago are: (1) Active immunization, so far as practicable, of groups of children in asylums, day nurseries and similar institutions. The use of the Schick test and the treatment with toxin antitoxin mixture of those reacting positively has given good results wherever applied. Adults especially exposed, as nurses, doctors and patients in contagious disease hospitals, should be treated with the Schick reaction and immunized when necessary. Extension of active immunization to all susceptible schoolchildren should be practiced wherever feasible.

(2) Special effort should be made to insure early treatment of all suspicious throat cases with diphtheria antitoxin. In many instances it is a waste of critical time to delay until the results of laboratory examination are available.

(3) The gravity of throat infections should be impressed on the whole community by newspaper and health department propaganda, by moving pictures and by education of the teachers in the public schools.

(4) Excessive prevalence of diphtheria in any school or in any particular district in the city should be made a matter of much concern and receive special investigation. Isolation and treatment of carriers, when found, is of high importance.

The committee believes that publicity should be given to these recommendations.

(Signed) T. R. CROWDER,
H. F. HELMHOLZ,
E. E. IRONS,
J. P. SIMONDS,
EDWIN O. JORDAN, Chairman.

ANNOUNCEMENT

The following have been elected fellows of the Institute:

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LOUIS PASTEUR

1822 — 1895

ETIENNE BURNET
The Pasteur Institute, Paris

Dec. 3, 1918

Pasteur was a chemist who brought about a revolution in the art of healing as momentous as any flood or glacial era ever produced in the formation of the earth's crust.

Our greatest scientist was, like your greatest statesman, Lincoln, of the most democratic ancestry. His father, Jean-Joseph Pasteur, having been conscripted in 1811, served under the Emperor Napoleon; every soldier of Napoleon was at heart a democrat, full of memories of the great revolution. These men always held that they were fighting in the cause of liberty.

In Pasteur, I find next an enthusiast and a sentimentalist. With the French peasant, sentiment is rarely apparent, yet rarely absent. Pasteur thought he had inherited his enthusiastic temperament from his mother. The day when a commemorative tablet was put up in front of the house where he was born, he said of his parents: "To you . . . I am indebted for all I am. You, my noble-hearted mother, kindled in me the fire of your enthusiasm, and you, dear father, whose existence was as toilsome as your toilsome craft, showed me what patience can achieve in long-protracted effort. To you I owe my tenacity in my daily toil. . . . To look ever upwards, to learn what lies beyond, always to strive after higher things, all this you taught me. . . ."

Pasteur was a keen patriot, and the disasters of 1870 filled him with poignant grief. I would especially emphasize the dauntless energy with which his soul strove to conquer that grief. It was borne in upon him that France had not merely been unfortunate, but guilty as well — guilty of having neglected the pursuit of knowledge. He wrote a few pages under the title: "Why France Found No Men to Lead Her in the Hour of Peril"; the cause, he wrote with blunt outspokenness, was the disdain professed by France, or by her government, for the high achievements of thought, more particularly in the sphere of exact science. He pointed out that during the wars of the revolution,

France owed her might largely to her scientists. After four years of war, the words of Pasteur appear to us as true as ever: "The development of science, in its highest expression, is perhaps even more necessary to the moral well being of a nation than to its material prosperity."

And the deep feeling that was in his soul, Pasteur brought into the pursuit of science. He speaks of the part played by the heart in the advancement of science. There has been no experimentalist more matter of fact, more careful or more precise, but it was by virtue of the love that was in him that those qualities accomplished great things. His soul shines forth more especially in his worship of letters, in his worship of great men. As a young student, he already looked on literature as the guide to general ideas. Enthusiasm for great men was, in his opinion, one of the foundations of education. The biographies of illustrious men should be, even in the elementary schools, among the sons of the people, the leaven of good thoughts and good deeds. Spellbound by the tale of Jenner's career, he urged wide dissemination of the life stories of such men, who leave in their wake a track of light.

By reason of the eager self-abandonment that he practiced in his thoughts and in his work, it may be said that Pasteur's life was one filled through and through with love.

To be a good son, a good brother, a good husband, a good friend—those are qualities not infrequently met with, and insufficient in themselves to confer immortality on him—were it not for the extraordinary soulfulness of the man, whereby they were immeasurably heightened. Those who knew him well marked the contrast between the simple, unassuming, nay diffident demeanor, and the depth of his soul, filled with volcanic flame and lava.

The essential trait of Pasteur's personality was his power. His power is made of two elements: A natural, vital energy that is indefinable; and an intellectual element, the assurance imparted to him by the experimental method of research. He said: "I am the most hesitating of men, the most fearful of the slightest responsibility, when proof is lacking. On the other hand, no consideration can prevent me from upholding what I consider to be the truth, when my convictions are grounded upon scientific proof." As he always did have scientific proof to hand, he was a formidable antagonist. In the pursuit and defense of truth, his power bordered on violence. He pos-

sessed the temperament of a conqueror. His power was so great, that however magnificent his intellectual parts, they were outdone by his persistent and masterful energy. When he had taken up a subject, he never left it. Attention had in him all the sustained intensity of a fixed idea. Whatever the stage that he had reached, he always wanted to go further. One of his maxims was: "It is no use being content with things already known." No new conception was too bold for him; he felt that even the strangest might be true, and the force that was in him urged him on to dare. His stubborn thought fastened on difficulties and eventually mastered them, just as the intense flame of a blow-pipe, if constantly directed on some refractory body, will end by melting it — so speaks of Pasteur his pupil Dr. Roux.

What was Pasteur's starting point? Pure chemistry. What his final achievement? A revolution in the medical art. There were four outstanding epochs in his work: molecular dissymetry, fermentations, infectious diseases, vaccinations.

The first work that made him famous was not even concerned with pure chemistry; it dealt with crystallography. He studied the salts of tartaric acid and found the relation between the shape of the crystal, their molecular structure and their power of rotation; that is to say, the power of deviating the plane of polarization of light. The study of the disposition of the atoms in dissymmetric molecules has given rise to a new science: solid or stereochemistry.

The substances which, when dissolved, act on polarized light have dissymetric molecules; and Pasteur said to himself that all these substances are organic products of vegetables and animals, that is, products of cellular activity. Nature builds up dissymetrical products. Again, when nature builds up mixed and inert bodies — like our paratartrates—she can separate them, suppress the one and leave the other. A mould, san Pasteur—a microbe—growing on a solution of inert paratartrate of ammonia, separates it into right-hand and left-hand tartrates, consumes the former as food, and leaves the latter.

Life consists of dissymetrical actions—all the universe is a dissymetrical whole. What would the world be like, were the earth to turn around the sun in the opposite direction to that it does? The very motion of solar light is dissymetrical. Could we not bring dissymetrical forces to bear on chemical phenomena? Pasteur brought powerful magnets to bear on certain crystals; he sought to make a

plant live from the time of its germination under the influence of solar rays reversed by means of a mirror actuated by a heliostat. It was in reference to these experiments that he said: "One has to be something of a madman to undertake them!"

Thus it came about that these investigations called his attention to the phenomena of life. Fate favored this new direction taken by his thought. He was appointed lecturer on chemistry at the University of Lille, which is located in a country where fermentations, and especially alcoholic fermentations, were the chief industrial activity. He was instructed to carry out a program that we could describe today as science applied to industry. But to his mind a scientific institute should above all seek out ideas. "Without theory," he observed to his pupils, "practice is mere routine. Theory alone can generate and develop the spirit of invention."

You have heard, of course, of Franklin's delightful retort when he witnessed the first demonstration of a scientific discovery. Hearing people about him ask: "But what is the use of it?" Franklin replied: "What is the use of a new-born child?" When he had thus duly set forth and acknowledged the rights of thought, Pasteur applied his theories, conducting his pupils to foundries, blast furnaces and distilleries. Here the second epoch of his career comes into view: fermentation.

The extraordinary part of the matter is that Pasteur—a chemist—finding the science of his time ruled by a purely physicochemical conception of fermentation, at once took the opposite standpoint and explained fermentation as a biologic phenomenon. In a vat in which fermentation is taking place, there is a liquid and a mass of more or less soft substances constituting the ferment proper.

In 1836, Cagniard-Latour, a Frenchman, examining this matter under the microscope, saw that it was composed of cells "capable of reproducing themselves by sprouting and probably acting on sugar merely by some effect of their vegetation." At the same time, one of the founders of the cellular theory, Schwann, declared these cells to be vegetable germs, that there was no fermentation when these cells are absent, and that the cell fed on the sugar and threw off in the shape of alcohol what they could not consume. Now for what reason had these observations and ideas remained a dead letter? Simply because the minds of the observers were turned in a different direction by a current of ideas that commanded attention.

"Fermentation is a catalytic process," said the Swedish chemist Berzelius; that is to say, it is brought about by an action of contact. What Cagniard-Latour and Schwann call cells, are deposits or precipitates that are vegetable cells in appearance only.

"Fermentation is a purely mechanical work," said Liebig. A ferment is matter possessed of a special motive power. Fermentation and putrefaction are started by a small quantity of matter in decomposition; the motion of which these decomposing particles of matter are possessed is communicated to the adjoining matter, which decomposes in its turn. Cagniard-Latour's and Schwann's cells really exist in the vat, but they are active when dead; they act as a ferment when they begin to decompose. Moreover, while they are to be found in alcoholic fermentation, they are not to be found in a quantity of other fermentations and putrefactions. What is required to start lactic fermentation? A small quantity of mouldy cheese. And butyric fermentation? A small quantity of putrifying meat. Liebig had no notion of the specific character of fermentations.

Why did Pasteur say that fermentation is effected by cells that live and multiply, not by dead cells in process of decomposition? He said this because he approached the problem with the idea instilled into his mind by his work on molecular dissymetry. In the case of alcoholic fermentation, amylic alcohol is produced, which deflects the plane of polarization of light. This product cannot be derived from the sugar by decomposition after Liebig's theory, for if so, it would no longer possess this power of rotation. And as it does possess that power, it must be a vital product and fermentation must be a vital action.

He then proceeded to study the manufacture of beet alcohol in a Lille factory. He examined the sweet juices, filtered and nonfiltered, and the cells they hold in suspension. The manufacturer in whose works Pasteur had set up his microscope and his little incubator saw thousands of experiments, countless alternations of enthusiasm and disappointment. The result of all this labor were the famous papers on lactic and on alcoholic fermentations. The former contains within its fifteen pages a multitude of ideas that shoot up like a luminous cluster of rockets — " a production of exuberant youth," says Duclaux, "in which you may still see his thought ferment and boil over. . . . During the best years of his life, this man lived in advance of his

time, like a pioneer merged in solitude, absorbed in the contemplation of the prospects he described and which his eye alone scrutinized and surveyed. Why should we wonder at his seeming indifference to matters pertaining to daily life?"

Fermentations are produced by micro-organisms; they are specific, each separate fermentation being the work of a special class of microbes; we thus have lactic fermentation, alcoholic fermentation, etc. We cultivate the ferments, we sow them, we gather them in, as we would any plant that we cultivate. We improve them by selection. There are some ferments that can only live if screened from the oxygen contained in the air; for them oxygen is a poison that kills. These ferments, known under the name of anaerobia, are those we found too often in gangrenous wounds during the great war.

Instead of the word fermentations, use the word diseases; for the word ferments, substitute the word microbes: "when we see beer and wine experience deep alterations from the fact that these liquids have given shelter to microscopic organisms which have come into them by chance and invisibly, and have there increased and multiplied, how can we help the thought from besetting us that the same kind of thing may and must sometimes occur in man and in animals?" The laws of diseases are the same as those of fermentations. Pasteur's ideas were soon to invade medicine.

Later, Pasteur again met scientists who did not believe that the living cell is absolutely necessary to cause fermentation. It was no longer Liebig, with his physicochemical theory by this time exploded, but men like Claude Bernard and Berthelot.

Berthelot believed in the existence of a soluble alcoholic ferment, capable of acting without the presence of living cells, and destroying itself as fast as it was formed. Pasteur at that time did not share this belief, but declared that his position would not be touched by the discovery of this ferment, for it would have to be admitted that this ferment must originally have been produced by living cells. Pasteur, himself, sought for it, and sought for it in the right direction; he used every possible means—crushing, congelation, extraction by means of saline solutions—to bring to light the soluble alcoholic ferment of yeast cells. In this, however, he failed, nor was it accomplished until after his death, by Buchner. There are, indeed, ferments that are soluble, but Berthelot was fain to admit that they are generated—

if not exclusively, at least for the most part — by some particular vegetable or animal. "The living entity is not the ferment, but generates it." Claude Bernard was quite right in saying that the phenomena occurring in living organisms are subject to the same laws as those that take place independently of life. As a chemist, Pasteur would have viewed these experiments as a continuation of his own. When later on he inoculated culture-broths freed by filtration of the bodies of microbes, what was it he was seeking after, but the very same soluble ferments sought for by Claude Bernard and Berthelot?

Whence come the ferments that are everywhere at work in nature? They are living cells that proceed from cells. They are never the result of a spontaneous process in decomposing matter. Enlightened by his research work on fermentations, Pasteur was able to solve this enigma, that through the ages has baffled the poets, the mystics and the men of science. Just as the lactic ferment is not produced spontaneously by mouldy cheese, so is it untrue that eels are born spontaneously of river mud; or that bees, as Virgil would have us believe, are born spontaneously of the entrails of a dead bull. Why were people still wrangling over this question in the middle of the nineteenth century when ever since the preceding century the experiments made by Spallanzani seemed to prove that there is no such thing as the spontaneous generation of living beings? It was for the simple reason that down to Pasteur's time experiments were wrongly conducted. It was he who made the final experiment, the experiment that in the history of science will ever remain as a masterpiece. What is there that is marvellous about it? Its simplicity.

The method of the experiment was briefly as follows: He said that in a portion of matter, fermentation or putrefaction will only set in if preexisting germs are introduced into it; no germs will ever be produced in it spontaneously. In a flask he placed a putrifiable infusion, stretched the neck of the flask into a long, thin, curved tube and boiled the liquid to kill the germs it contained. He left the recipient to itself. No fermentation or putrefaction occurs.

Yet the liquid is in communication with the outer air, and there is no lack of oxygen, since the neck of the flask is not closed, but when the flask has cooled off and a little of the outer air has entered it, the germs contained in the air have settled on the moist walls of the neck without reaching the liquid.

His chief antagonist, Pouchet, might raise the old objection, that the heating had destroyed a certain mysterious vital force that was in the liquid. Pasteur said: "That is not true, for I can make it ferment whenever I please. I have but to cut off the neck of the flask and let the dust that is in the air fall into it, together with the germs it contains. Nay, more, I cut off nothing, I touch nothing, I merely incline the flask sufficiently for the liquid to reach the part of the neck where the germs of the air have settled and let it flow back into the flask, which is now contaminated; fermentation sets in."

This flask has become famous in the annals of science: it is known as Pasteur's swan-neck flask. At the Pasteur Institute several of these flasks are preserved as precious relics; they were used for the foregoing experiments and have never corrupted.

The germs that set up putrefaction and fermentation are everywhere present in nature: in the air, in the water, in the earth; and Pasteur showed how they are to be found there. There are, moreover, in the air and in the water, certain germs or microbes that engender diseases. Pasteur's experiments on spontaneous generation, the organized corpuscles of the atmosphere and the sterilization of liquids, gave birth to modern hygiene.

We have hitherto made no mention of medicine — yet the problems of medicine confront us at every turn. How was Pasteur led to deal with the problems of medicine?

Let me take you back to about the year 1860. There were men, on the one side, whose profession it was to study and to cure disease. Now, contagion and infection were mysteries beyond their ken. It was known, indeed, that the itch was caused by the presence in the skin of a small parasitic animal, but to nobody did it occur that there were parasites of typhoid fever and tuberculosis. Your true physician, at that time, had no use for physiology or chemistry; sciences he looked on as quite superfluous, as far as the art of healing was concerned. The mere notion that diseases may be due to specific germs was enough to frighten him. Tuberculosis, to quote a famous professor of the period, was "the common termination of a number of different causes, internal and external, and not the product of a specific agent, always the same." "Applied to chronic diseases the specific theory leads us to the research for specific remedies or vaccines, and all progress is at an end."

When, one day, Villemin proved experimentally that tuberculosis could be inoculated from one animal to another, Professor Pidoux fondly thought he had cornered him by holding up to him as an absurdity a consequence which today is common sense pure and simple. "Then nothing is left to the doctors but to cast their net to catch the germs of tuberculosis, or to discover the vaccine. . . ." Diseases were wrapped in mystery, governed by fatality as in the days of antiquity.

Now as against these high priests of official medicine, there appeared a chemist who had made it his business to study crystallography and fermentation. He had never set foot in a hospital, but his discoveries and the natural bent of his genius urged him toward biology and medicine. The microscope that served him to examine his little crystals of tartaric acid, and then to observe the yeast cells, were soon brought to bear on tissues and on the blood. This microscope may be likened to the astronomic mighty telescope pointed at the sky in the right direction: the stars *must* pass in front of it. He knew that there are certain alterations in wines, beers and vinegars, due to the fact that normal fermentation is supplanted by vicious fermentation; mischievous ferments, or in other words, evil microbes, take the place of the good ones; the wines, beer and vinegar then suffer from actual diseases — and he knew how to *cure* them!

Then (from 1865 to 1870) he worked out these intuitive forecasts; he studied an infectious and contagious epidemic disease, discovered the cause of it, and taught how to guard against it. Does this mean that he studied a great human epidemic? Nay, for his master, J. B. Dumas, had asked him to study a disease that attacked silkworms.

The spots that appear on the body and in the organs of diseased silkworms are parasitic microbes. By these the disease is transmitted to the neighbors; it is a contagious disease. The microbe passes from the worm to the chrysalis, and from the chrysalis to the moth; it is a hereditary disease. Pasteur said the diseased worm must not be allowed to develop; only the products of noncontaminated eggs must be reared. The hereditary disease is thus suppressed. Separate, isolate the healthy worms from the sick ones you thus suppress contagion.

Yet when Pasteur approached this work, he was no more of a zoologist than he was a physician. It was only a few days before he

left for the south that he first dissected a silkworm. A second disease added a fresh complication to the one he was studying; and, while increasing the difficulties, only had the effect of enlarging the scope of the discoveries. Pasteur was guided in his investigations by his ideas on fermentation and by the experimental method. He gained the mastery over the disease and was in a position to say that "it was as easy to prevent as to communicate." After approving himself an inventor, he turned apostle, journeying from town to town for the purpose of teaching his method of sorting out the eggs.

After thus investigating the phenomena of fermentation and the diseases of silkworms, Pasteur was the only man in the world in a position to give a scientific and complete explanation of infectious diseases and to find the vaccines against microbes.

Far from being lessened, his genius stands forth all the more when his work is considered in relation to what other men were doing at the same period.

It was not Pasteur who discovered the existence of microbes. As soon as the microscope was invented in Holland, naturalists such as Loewenhveck described some of them, and Ehrenberg was studying and classifying many of them when Pasteur was still a boy at school, but nobody had the faintest conception of the part they play in fermentation and disease. That idea was contributed by Pasteur.

It was not Pasteur who first discovered parasitic diseases, but to those who observed the presence of an Acarus in the itch, this parasitism appeared merely as a peculiarity that they never dreamt of applying in the study of infectious diseases. To have conceived and demonstrated that infectious diseases are fermentations occurring in the bodies of animals and plants, for this we are indebted to Pasteur.

In 1850, for example, Rayer and Davaine discovered a filament in the blood of animals attacked by anthrax; in 1860, Delafond went so far as to conceive that these filaments are living vegetable cells, capable of growth, of yielding a "culture," as it has since been called. However keen their insight, none of these observers dares to say: This vegetable cell is the cause of the disease. Why was Davaine bold enough to say some twelve years after his earliest observations: Anthrax is a contagious disease caused by the presence of these cells, the bacilli of anthrax? It was because in 1861 he had read Pasteur's papers on lactic and butyric fermentations.

Why was it that all the discoveries in various diseases still left a doubt in the minds of scientists? It was because the demonstration of the pathogenetic action of microbes was not compelling; it was experimental. The convincing demonstration was supplied by Pasteur in his experiments on anthrax.

Robert Koch had cultivated the bacillus in a liquid drop, with which he could inoculate the disease. His contention, therefore, was that this cultivated bacillus is unquestionably the cause of the disease. "Not so fast," declared his obstinate antagonists. "There was perhaps in the blood used for your culture some poison which you introduced into the drop, and which had remained sufficiently active to produce the disease." But Pasteur intervened with his huge dilutions in a series of flasks—as large and numerous as might be desired; the original drop of blood may be diluted in a volume of liquid as huge as the volume of the earth, yet a drop from the last flask imparts the disease. It is no longer a question of poison; there has been effected a culture; and in the last broth there is nothing but the microbe that can produce anthrax.

There were men in Pasteur's time who discovered and cultivated microbes. But he is far ahead of them all by virtue of the idea, because he found the secret of fermentation. While Pasteur was engaged in the study of anthrax, other scientists, notably R. Koch, also made beautiful discoveries. Pasteur, however, is again ahead of them all with the idea; none but he was great enough to create the attenuation of the virus and vaccinations.

The cultivation of the bacillus of anthrax in a drop of liquid; the discovery of the spore, which is the element of resistance and, as it were, the seed of the microbe; the perfecting of bacteriology, which in his hand became a practical instrument of medical research: this is the work of Koch.

But to have observed that microbes grown old produce a comparatively slight disease; that this disease renders the animal refractory to a more severe inoculation; to have discovered these facts in connection with a disease pertaining to farm-yard poultry, the so-called fowl's cholera, and to have applied them to the treatment of anthrax; to have created in the laboratory attenuated microbes; to have played, as it were, with the virulence of disease, raised or lowered it at will; to have taken up the work of Jenner and prepared vaccines that can

be sent to the other end of the world and which the humblest veterinary surgeon can inoculate with a syringe to ward off disease from animals and men — this was the achievement of Pasteur!

In the discovery of vaccines and attenuated viruses, I see yet another instance of that force of sentiment, of that wilful energy, which in Pasteur goes beyond the limits of the purely intellectual faculties. The discovery of vaccines is the product of sentiment and a fixed idea, with his passionate admiration for great men. Pasteur had read and reread the life of Jenner and meditated deeply on the immortal discovery of smallpox vaccination. As soon as he laid his finger on the cause of infectious diseases, he strove to prevent them by vaccination. Just as, when confronted with an unexplained disease, he would repeat untiringly: "The microbe must be sought for"; so, when the microbe was known, he would keep on repeating: "Now a vaccine *must* be prepared." In 1857, there was but one man in the world capable of accomplishing the work on lactic fermentation. In 1875, there was but one man in the world in whose mind and soul was this deep-rooted idea: Vaccination must be used against infectious diseases.

The spirit of unbounded energy, I might even say the spirit of daring and adventure, characteristic of Pasteur, is made manifest in the celebrated experiment that allowed antianthrax vaccination to enter on the practical stage. The Agricultural Society of the Seine-et-Marne department requested Pasteur to test his method on two lots of sheep, prevising that all the animals inoculated were to be immune, while all those not inoculated were eventually to succumb to anthrax. This program Pasteur accepted. His pupils and fellow-workers, Roux and Chamberland, were at the time away on their vacation. When they came back they were somewhat frightened at the rigorous conditions laid down for the experiment. "I have signed my name," said Pasteur, "there is nothing for it but to set to work." During the weeks of suspense, however, when it came to taking at regular intervals the temperature of the sheep inoculated, then of the sheep attacked by the virulent inoculation, Pasteur was very anxious. He had *never* played for such high stakes. But he won; and on the day of victory, ignoring or forgetting the anxieties he had experienced, and carried away by the elation of success—after the manner of a conqueror—to those who confessed that they had had their fears as to the result, he replied with the biblical phrase: "Ye men of little faith! . . ."

The same impulsion of genius that led Pasteur to develop vaccination, led him even farther than the realm of infectious diseases to that of toxical diseases. When his pupil Roux demonstrated that diphtheria is a toxemic disease, a disease in which the microbe does not invade the organism, but acts at a distance by the poison it secretes, and when he had isolated the diphtheric poison, it was again Pasteur who said: "Now we must vaccinate against the poison as well." His finger pointed to the road along which serum therapy was discovered.

Finally this genius soars to an unbelievable, paradoxal height in his work on hydrophobia. With Roux as a collaborator, Pasteur contrived to transmit rabies experimentally with a minimum and constant period of incubation; he created the fixed virus; sought for the microbe, but did not find it — nor has it yet been discovered; but he said to himself that in a disease like this, which is a nervous disease, the virus should be located in the nervous system. He took the nervous system as a culture of the rabic virus in the living being himself; and handling that virus without seeing it, he managed to attenuate it, and invented antirabic vaccination. In no science was there over achieved so stupendous a masterpiece of experimental work.

It was especially after this discovery of the treatment of rabies that pasteur was admired by the whole world, and almost deified in France. And indeed to us his work is that of a demigod. The words of Emerson occur to me: "All mythology opens with demigods."

Pasteur's ideas led in the end to practical consequences; they are levers that always find a fulcrum in the material world. His thought travels — as Heine said of Napoleon — with seven-league boots. I would fain give you a few instances of these very simple ideas that have transformed entire regions of science and life.

He observes that when a silkworm moth is but little infested with "corpuscles" (or parasites), its seed (or eggs) will produce worms exempt from corpuscles, or exhibiting these quite exceptionally, at the end of their lives. This immediately gives him an intuition concerning tuberculosis in man.

He said: "Were a number of children born of parents suffering from pulmonary consumption to be collected in one place, they would grow up more or less sickly, but would only exhibit to varying degrees and at different ages the pulmonary tubercles that are the infallible sign of their bad constitution. Things go on much in the same way with silkworms."

To show that grapes do not ferment unless they take with them into the vat ferments sown on their skins, he wrapped in sterilized cotton-wool some of the grapes of a vine, at a time of the year when there were as yet no ferments on the bunches of grapes. In autumn the grapes not wrapped up in this way bore yeasts and ferment; those wrapped in cotton-wool did not ferment. To Pasteur's mind this cotton-wool becomes an aseptic dressing such as we apply to the wounds of the soldiers; it becomes a sanitary barrier, such as we set up against epidemics. Let me tell you his own words:

"What food for thought do these results afford us, and how are we to help observing that the farther we proceed in the experimental study of germs, the more glimpses do we obtain of unexpected shafts of light and accurate notions as to the causes of infectious diseases! . . . These few cubic feet, these few square feet at the surface of the ground (where grew the vine) were there right in the middle of possible contagion from all around, yet they had for several months had nothing to fear on that score. . . . Is it not permissible to believe, by analogy, that the day will come when preventive measures of easy application will arrest these plagues which suddenly afflict and terrify the populations: yellow fever, for instance, which has recently invaded Senegal and the valley of the Mississippi, or the bubonic pest which has broken out on the banks of the Volga?"

Pasteur had discovered the existence of the microbes pervading the air, the soil, everything that is around us and in contact with us. He had discovered the anaerobia of putrefactions; he had observed that certain wounds are invaded jointly by aerobia and anaerobia. He had even inoculated experimentally his "septic vibrio" into healthy muscle; the flesh became gangrened, green at the surface, swelled up with gases, and readily gave off a loathsome, sanious discharge—the type of the gaseous gangrene so frequent in the war. From this starting point he proceeds swiftly, and draws up in one page *the whole program of modern surgical asepsy.* That page will live forever:

"Had I the honor of being a surgeon, penetrated as I am with the dangers resulting from the germs of the microbes settled on the surface of every material object, especially in the hospital, not only would I use none but instruments of perfect cleanliness, but after washing my hands with the greatest care and subjecting them to a rapid flaming, no more painful a process than when a smoker passes a live coal from

one hand to the other, I would restrict myself to the use of lint, bandages, and sponges previously exposed to an air heated to a temperature of 230-270 F. I would never use any water that has not been boiled. All this is quite practicable. In this way the only germs I should have to fear would be those floating in the air round the patient's bed; and observation shows us every day that the number of these germs is practically insignificant as compared with those pervading the dust on the surface of material objects, or the very clearest ordinary water."

Pasteur's discoveries had suggested to Lister the antiseptic treatment. Pasteur went farther, while simplifying the process, and created the aseptic method from which resulted modern surgery.

Pasteur's work was mainly achieved in his mind and thought; but an experimenter needs laboratories. At Strassbourg and Lille he had at his disposal modest laboratories, very primitive no doubt as compared with these we see today, but fairly adequate on the whole. When he returned to Paris, the only chemical laboratory existing at the Ecole normale was used by Sainte-Claire Deville. This illustrious chemist occupied a few ill-lighted rooms, containing very few apparatus, and the funds allotted to him every year for the prosecution of his work amounted to 1,800 francs, about $360. As to Pasteur, he was obliged to set up a laboratory in a corner of a garret, in two uninhabitable and unused rooms. He had no assistant. Here it was that he concluded the work on alcoholic fermentation. When he wanted to enter the incubator room he had installed by dint of ingenious shifts, he could only do so on his knees. "Yet I have known him to work there for hours," records his pupil Duclaux, for it was in this tiny incubator room that he prosecuted all his investigations into spontaneous generation. From this hovel that would hardly serve today as a rabbit hutch, started the movement which has revolutionized in its every aspect the science of physical man."

Napoleon III and his minister, Duruy, eventually ordered the construction of a better laboratory, the building that stood for many years in front of the Ecole Normale supérieure at Paris. The minister of education and the emperor's household in their joint generosity contributed 60,000 francs, $12,000.

It was Pasteur's mighty voice that was raised most eloquently in support of the institution of laboratories in France. After his dis-

coveries concerning hydrophobia, an international subscription yielded the sum of 3 million francs, $600,000, considered a huge sum in Europe at that time. The Institut Pasteur was opened on Nov. 14, 1888.

In France, centralized as regards her administration by Napoleon, the Institut Pasteur embodied this paradox: an institute independent of the state, created by private means. In such a foundation there is nothing to astonish you; you have hundreds of them in this country. In our land, where the vestiges of monarchy and of the empire are so slow to disappear, it took a Pasteur to create this institution. It is not excessive to say that this was the crowning achievement of his genius.

"It is my intention," he had said, "to found in Paris a model establishment without applying for state support, with the help of international gifts and subscriptions."

It was Pasteur himself who dedicated his Institute by delivering the following speech on the day of the opening. More than ever these words express our common faith.

"Two conflicting laws are now arrayed against one another: a law of blood and death, which by daily devising fresh means of combat, obliges the nations to be ever in readiness for the battlefield; and a law of peace, work and salvation solely concerned with freeing mankind from the ills that beset us.

"The one aims only at violent conquest; the other, at ministering to suffering humanity. The latter holds human life more precious than any number of victories; the former is ready to sacrifice hundreds of thousands of lives to the ambition of one man. The law whose instruments we are strives even in midst of slaughter to cure the sanguinary evils of that law of war. The dressings inspired by our method (antiseptics) may save thousands of soldiers."

"Which of these two laws will prevail over the other? God alone can tell. But what we may safely assert is that French science will have endeavored, by obeying this law of humanity, to lengthen the span of life."

Frederick Gillette Harris, 1874-1919

FREDERICK GILLETTE HARRIS
1874–1919

Dr. Frederick G. Harris died at his residence in Chicago, July 2, 1919. His death was due to pneumococcus meningitis. For a few days preceding his illness he complained of headache, and of not feeling well. He worked on, as he had done innumerable times before under similar conditions. On Monday, June 30, he went to bed; the next day evidence of meningitis developed and on Wednesday he was dead. Early in the war he tried to enter the army and was rejected on account of a mitral lesion, which until that time was unknown to him. It is not unlikely that his meningitis was a sequel of this.

Frederick Gillette Harris was born in Chicago, Oct. 19, 1874, and Chicago remained his home during his lifetime. He was graduated from the West Division High School in June, 1895. The following autumn he entered the School of Medicine of the University of Illinois from which he graduated with honors in 1899. In June, 1900, he became intern in Cook County Hospital. On finishing his internship, December, 1901, he was appointed resident pathologist at the hospital, which position he held until June, 1903. This position, which is that of house-officer to the attending pathologist, gave him access to a great quantity of postmortem material. As a result of this experience, and of his continued interest in pathology after giving up his position as resident pathologist to the hospital, he became an expert dead house pathologist with a very extensive first hand knowledge of pathologic anatomy.

He spent the next year in Vienna and Berlin and Paris as a student of general medicine. Returning to Chicago in the fall of 1904, he was appointed, first, adjunct professor of physical diagnosis, and later, adjunct professor in medicine in the University of Illinois. He spent a year during 1907 and 1908 in the study of dermatology in Europe, and returning to Chicago in 1908, he thereafter devoted his time to dermatology. He was at once appointed instructor and later assistant professor of dermatology in the University of Illinois. In 1917 he became professor of dermatology and syphilology at Northwestern University. At the time of his death he still held this position together with that of attending dermatologist at Wesley and Cook County Hospitals. He was a member of the American Dermatological Association.

Throughout his professional career he was connected in one capacity or another with Cook County Hospital, the great reservoir of clinical material in Chicago. A feat indicating his competency in general medicine was that of obtaining on civil service examination in 1906 a position as attending physician on the Cook County Hospital staff. At that time, in order to avoid the abuse of political influence in appointment of members of the attending staff of the Cook County Hospital, the positions were placed under civil service and awarded by competitive examination. It was a new order of things in the County Hospital, and the positions were sought by the best men in Chicago. In competition with a hundred or more of such men in internal medicine, Harris received sixth or seventh place as an attending physician. He obtained his position as attending dermatologist in the Cook County Hospital under the same conditions in 1912.

After his first training in dermatology, Harris became one of the dermatologists of respected ability of Chicago. He was an indefatigable clinician. He was seeing a large amount of material all of the time, and was always presenting cases and calling attention to points in them which were interesting and often puzzling to us. In addition to this, he knew so much general medicine and pathology that his views were given more than ordinary respect. He was always in attendance at the Chicago Dermatological Society, where he showed many interesting cases and was in all ways one of its best members. He was president of the society in 1915. He was one of the pioneers in this country in the use of the serum reactions in syphilis, and in the study of the spirocheta pallida.

He was not a prolific writer, but he was a regular contributor to dermatologic literature. His papers showed the qualities that would be expected of him. They were sound and scientific with a leaning toward the laboratory. His thoroughness and learning are well illustrated in his paper on the etiology and pathology of cancer of the skin, which he read in opening the discussion on cancer at the meeting of the American Dermatological Association in 1917.

Harris' great knowledge of medicine was the result of a clear mind and of unending work. He habitually began his labor early in the day, usually worked until evening without intermission for lunch, and as a rule continued late into the night. He had a frail body, and his exacting demands on himself more than once led his friends to protest to him. It cannot definitely be said that over-work killed him, but he

did work too hard to keep up his resistance, and it is probable that overwork was a contributory cause of his untimely death.

While his consuming interest was medicine, he had diversions to which he allowed a little time. He enjoyed motoring and took frequent trips into the country or to points of interest in the district surrounding Chicago. His favorite trip for a day was to the dunes on the southwest shore of Lake Michigan, a region of fascinating interests which Harris was capable of appreciating and thoroughly enjoyed. He was fond of travel, and his vacations were often spent in some part of the Rocky Mountains. He was an active member of the Chicago Geographical Society and a constant attendant at its lectures. He also had a lively interest in the history of the middle-west, and was an active member of the Chicago Historical Society.

Harris had expected to devote his life to internal medicine, but in 1906 he thought he saw intimations of middle-ear deafness which threatened his career as an internist. Happily this never developed, but it was at my solicitation, on learning this, that he decided to become a dermatologist. He came with me as my associate in private practice, and remained with me for about a year. The association was delightful; no dermatologist ever had a better assistant or a more congenial companion. He was always agreeable. An intimate association with him for many years disclosed no qualities to interfere with his likableness. He was modest and quiet and unassuming. He was not temperamental or demonstrative, and, if he had moods, he did not disclose them. His ideals and his personal and professional standards were exacting of himself, but I can remember no instance where they were not generous in his judgment of others.

Measuring him in the most critical way, he was an admirable man and a physician of the highest class. He was a colleague who cannot be replaced. His death relatively early in his career is a loss to American dermatology.

WILLIAM ALLEN PUSEY.

EXPERIMENTAL STUDIES IN DIET DEFICIENCY DISEASES

JOSIAH J. MOORE
Oct. 30, 1919

Although numerous experiments concerning the value of food substances had preceded the war, this catastrophe gave the impetus which has made the consideration of food and diet in a broad sense a most important subject at the present writing. Outbreaks of scurvy among the British troops in Mesopotamia led directly to the establishment, at the Lister institute, of a corps of workers to study its prevention. The huge number of cases of night blindness, war "edema" and scurvy among the civil population of countries with inefficient food supplies, focused the attention of physicians the world over on the value of an adequate ration. With such a stimulus urging on workers in all parts of the world it may be conservatively stated that the study of the efficiency of foodstuffs and diets surpasses in immediate interest that of almost any other single subject.

During the last few years, many investigators have been studying the effects of food substances on other grounds than their relative caloric value. These experiments have developed along two paths. The first, as brought out by Osborne, Mendel, and their co-workers, demonstrates that certain proteins may be deficient as a ration in that they are lacking in necessary amino-acids. The second, that when some animals are fed on a diet consisting of pure proteins, carbohydrates, certain fats and salt mixture of appropriate compositions, normal growth fails after variable periods, and in addition the animals may show the pathologic manifestations of a definite disease. Such a diet, although fulfilling all the energy and caloric requirements, is inadequate to maintain normal growth or prevent pathologic changes. This second insufficiency in the diet has now been fairly well proved, by a large group of workers, to be due to the lack of certain essential substances which have been given various terms, such as vitamins, growth determinants, accessory food substances, and, according to their solubility in fats or water, fat soluble A, water soluble B, and water soluble C.

The majority of the earlier experiments in testing the efficiency of a diet were carried on with the white rat. This animal consumes a

small amount of food, matures early, and can be studied over long periods with comparative ease. It is subject to one so-called "diet deficiency" disease, a soreness of the eyes which may go on to blindness, termed by McCollum[1] xerophthalmia. This condition is readily cured when butter fat is added to the ration; the essential substance is termed fat soluble A by McCollum. Eijkman,[2] Funk[3] and others have produced a polyneuritis in birds closely resembling beriberi by feeding polished rice. This is relieved by the introduction of water extracts of several natural foods into the diet, such as yeasts and oats, and the essential substance is termed by McCollum, water soluble B. Funk has designated these antineuritic and antiscorbutic substances vitamins, and the diseases arising from their absence or insufficient amount, deficiency diseases or "avitaminoses."

In 1907 Holst and Fröhlich[4] produced a condition in guinea-pigs which resembles infantile human scurvy, by feeding oats, bread and unpealed grains. The clinical symptoms in brief are: Marked tenderness of the wrists and knees at first, followed by swelling of these joints and of the costochondral junctions, ankle and elbow joints, with occasional swelling of the gums, and dullness of the lower incisors. The bones become fragile so that fractures of the long bones are not rare. The swollen hind legs are usually so painful that the animal cannot walk. Death occurs in from four to five weeks. The chief pathologic lesions are hemorrhages around the joints and costochondral junctions, in the bone marrow, tooth pulp, skin, gums, muscles, lymph glands, intestines and other organs. The molar teeth are usually very dark in color, and so loose that they can be easily removed. The ends of the long bones, especially the lower ends of the radius and ulna, and the upper end of the tibia, and costochondral junctions are enlarged.

They observed further that the condition could be prevented or cured by feeding fresh vegetables. These observations have been so frequently confirmed that the guinea-pig, in which experimental scurvy can be readily induced, prevented, or cured, is now the animal of choice in estimating the antiscorbutic value of foodstuffs.

[1] The Newer Knowledge of Nutrition, 1919.
[2] Arch. f. Hyg., 1906, 8, p. 150.
[3] Die Vitamine, 1914.
[4] Jour. Hyg., 1907, 7, p. 634.

A similar condition has been induced in the monkey by one-sided diet,[5] but the difficulty with which they are obtained and the long periods over which they must be fed, has led to their infrequent use.

Since cow's milk plays such a large part in the dietary of man, it is natural that it would be one of the first foods tested to ascertain its value in respect to the essential substances just discussed.

Bolle,[6] as early as 1903, called attention to a condition in guinea-pigs having many features similar to infantile scurvy, which was produced by feeding raw milk. Bartenstein[7] and Fröhlich observed similar changes. On the other hand, Funk[8] prevented the onset of scurvy by feeding guinea-pigs 50 c c of uncooked milk in addition to an oat diet. Hopkins,[9] by giving as small a quantity as 2 c c of milk to white mice on a diet of purified foodstuffs, promoted growth when with no milk the animal lost weight. Osborne and Mendel[10] conclude that in feeding white rats, milk food contains all that is essential for growth and maintenance. Vaughan,[11] in a series of experiments to test the injurious effects of liquor formaldehydi when added to milk, states that "milk that had no formaldehyde in it had just as injurious an effect and killed just as quickly as the milk with formaldehyde in it."

In our laboratory, for over five years, we have been producing the clinical symptoms of experimental scurvy in young guinea-pigs on a diet of pasteurized Chicago market milk ad libitum and timothy hay. The condition, although not as severe, since the teeth seldom become loose and the animals usually survive, is clinically and pathologically similar to that produced by an oat diet. As shown by Dr. Jackson and myself,[12] the histologic picture of the two conditions are the same. Lesions produced by feeding milk boiled for ten minutes were of the same degree and type. It is to be expected that pasteurized and boiled milk may cause experimental scurvy, since the treatment to which milk is subjected will destroy the antiscorbutic substances. These results confirm those of Hess[13] in which babies fed on milk pasteurized for thirty minutes at 140 F. developed a more or less marked form of scurvy.

It is now generally conceded that when guinea-pigs are fed a diet of boiled or pasteurized milk ad libitum with hay, mild or severe

[5] Harden and Zilva: Jour. Path. and Bacteriol., 1918-19, 22, p. 246; Hart and Lessing: Der Skorbut der kleinen Kinder, 1913.

[6] Ztschr. f. diätet. u. physik. Therap., 1902, 3, p. 354.

[7] Jahrb. f. Kinderh., 1905, 61, p. 22.

[8] Biochem. Jour., 1913, 7, p. 81.

[9] Jour. Physiol., 1912, 44, p. 425.

[10] Jour. Biol. Chem., 1913, 15, p. 311.

[11] Jour. Am. Med. Assn., 1916, 67, p. 1934.

[12] Jour. Infect. Dis., 1916, 19, p. 478.

[13] Jour. Am. Med. Assn., 1916, 68, p. 235.

experimental scurvy will develop, but there is at present much controversy over the antiscorbutic value of raw cow milk. Bartenstein and Fröhlich both noted that 50 c c of raw milk protected a guinea-pig when fed on an oat diet.

Barnes and Hume[14] state that from 100-150 c c of raw milk daily is necessary to prevent scurvy in animals weighing from 300-500 gm. when fed from 10-20 gm. of oats and bran. They find that "the experiments with guinea-pigs are extremely difficult to carry out. Few animals of this size are able to tolerate these large amounts of fluid without digestive disturbances."

Hess and Unger[15] found that 80 c c of raw milk prevented scurvy in their guinea-pigs, while Hart, Steinbock and Smith[16] got protection when the fresh whole milk consumed daily per individual equaled 60 c c or more.

In our experiments in feeding raw milk of two types, Chicago certified and the so-called "baby" milk ad libitum with dried hay, mild scurvy has occurred in all animals weighing under 150 gm., and in the majority of those of larger size. The average daily individual consumption of some animals was 100 c.c and 115 c c, showing that such amounts of the milk used was deficient as an antiscorbutic. The occurrence of scurvy with an oat diet could not be prevented by adding milk ad libitum. However, on the mixed diet it took longer for the symptoms to appear, and they were of a milder type than when the diet consisted solely of oats and hay.

Raw milk without the addition of hay or oats is a very unsatisfactory diet for guinea-pigs. They usually die during the first week. Some, however, have lived for over thirty days, but even with such a large daily intake as 150 c c of milk per day they fail to gain consistently in weight, the abdomen is greatly distended, and finally death ensues, but with no gross lesions of scurvy.

Condensed milk diluted with an equal quantity of water and fed with hay produced severe scurvy. Four proprietary baby foods all caused severe scurvy when unmodified. When cow milk was added, life was prolonged, but scurvy appeared in all instances. Wheeler and Biester[17] have found that two of these foods, composed of cereals

[14] Lancet, 1919, 197, p. 323.
[15] Jour. Biol. Chem., 1919, 38, p. 293.
[16] Ibid., p. 305.
[17] Amer. Jour. Dis. Child., 1914, 7, p. 169.

and milk, were sufficient for the maintenance and growth of white mice for relative long periods. Mice fed on foods containing no milk lost steadily in weight.

We are now in a position to explain partially the somewhat divergent results obtained by feeding milk and certain milk products. They may be considered under four headings: (1) The species of animal and the age and individual variations in that species; (2) the diet and physical condition of the cow producing the milk; (3) the freshness and treatment of the milk, and (4) the value of milk as a supplement to deficient food mixtures and the total quantity of milk consumed.

(1). Variation in species of animals.—A diet which is sufficient for growth and maintenance in one species may be either similarly adequate for another,[18] may be sufficient for maintenance only, or may produce one of the so-called deficiency diseases.

The fact that rats and mice apparently do not get scurvy makes such animals of no value in testing the antiscorbutic properties of food. Comparing the work of Wheeler and Biester[17] with ours in the feeding of proprietary infant foods, we find that those foods entirely adequate for rats are entirely inadequate for guinea-pigs. Diets which maintain cows for months, will produce scurvy in guinea-pigs in a short time. The guinea-pig is the most susceptible species to lack of antiscorbutic vitamins. Hess reports that in order to cure guinea-pigs with scurvy they must be given 1.5 c c of orange juice a day, while the much larger human infant will do well on 10 c c per day. With our present knowledge, it must be strongly emphasized that results obtained with a single species cannot be applied generally to all species.

As noted, a few of our animals on the milk and hay diet grew normally with no symptoms of scurvy, while others died in a relatively short time of the disease. The young animals with their greater nutritional requirements for growth and maintenance were most susceptible to the deficiencies. It has been noted in our experiments and by others that individual animals may appear to grow well for a long time on a diet which does not at all maintain others of the same species and of approximately the same size.

(2). The diet and physical condition of animal producing milk.—Several authors[19] have noted that milk at different seasons varies in its antiscorbutic properties, and that spring and summer milk, when the

[18] Hart and McCollum: Jour. Biol. Chem., 1914, 40, p. 378.

[19] Dutcher, Pierson, Biester: Science, 1919, 50, p. 184; Barnes and Hume; Lancet, 1914, 197, p. 323.

cows are fed on green grass, is more potent in this respect than the winter milk. Milk from mother guinea-pigs on a scurvy producing diet will not prevent scurvy in the nursing young in all cases. Many authentic cases of nursing infants getting scurvy while on breast feeding are on record. The studies of Andrews,[20] showing that infants nursing mothers suffering from beriberi may develop beriberi, and that when these mothers were induced to nurse puppies the latter had symptoms somewhat similar to beriberi in man, are all confirmatory of the idea that inadequacy of the essential food substances in the diet will cause a lack of such material in the milk.

It is possible that a diseased condition of the cow other than that arising from a deficient diet may decrease the vitamins in milk. This may be a partial explanation of the outbreak among guinea-pigs reported by D. J. Davis and Moore[21] in 1912. These animals were fed on a general diet supplemented with milk from a cow suffering from experimental streptococcal mastitis. The majority of the young guinea-pigs developed scurvy. Knowing the unstability of the water soluble vitamins of milk, it may be surmised that these substances were either partially or wholly destroyed by the infection. A more complete investigation of this point is now under way.

(3). Freshness and treatment of milk.—All handling of milk, such as pasteurizing, boiling, condensing, drying or the incorporation of milk into other products where heating is necessary diminish to a marked extent the antiscorbutic properties for guinea-pigs and infants. Pasteurizing and aging are very pernicious in the destruction of these qualities as Hess and Unger[22] show in their work on babies and animals. In all our experiments with raw milk, in order to test the actual antiscorbutic value of the milk as delivered for consumption, the Chicago market raw milk was employed. It was at least 24 hours old. It is to be expected that fresh cow's milk a few hours old would make a better showing.

(4). Milk as a diet supplement and quantity of milk consumed.—The ideal diet for producing experimental scurvy—oats, hay and water —is not in itself an adequate food, being deficient in mineral matter, protein mixture, fat and the fat soluble vitamins. The cow, pig and white rat, apparently insusceptible to scurvy, will not grow and reproduce normally on the oat seed as the sole nourishment. The addition

[20] Philippine Jour. Sc., Ser. B, 1912, 7, p. 67.
[21] Trans. Chicago Path. Soc., 1914, 9, p. 185.
[22] Jour. Am. Med. Assn., 1919, 72, p. 1185.

of milk which has a satisfactory amount of salts, fats and proteins makes a combination which is entirely satisfactory for rats and pigs. Milk and whey proteins have been found to be the most effective supplements of the cereal proteins, such a mixture causing a decided increase in the nitrogen retention of the growing animal (pig).[23]

In the deficiency disease termed xerophthalmia, occurring in rats from lack of fat soluble vitamin, it is found that with all the dietary factors in abundance over the minimal requirements, the disease can be prevented by introducing a minimum of the fat soluble essential; lowering the protein, however, will cause the disease to appear. The diet can be adjusted so that either increasing the protein or the fat soluble A content of the food will relieve the condition (McCollum[1]).

Such facts are confirmatory evidence that a diet must be adequate in all other constituents in order to test the deficiency of one. It is only when such a state exists that the minimal quantity of the deficient substance will be required. This observation, with the fact that milk will cause an increased nitrogen retention and better growth, may offer an explanation of the lengthening of the latent period, of the milder form of the disease, and the production of the chronic type when oats are supplemented with milk. The English investigators, Chick, Hume, and Skelton,[24] add weight to this hypothesis by stating that "it was necessary that the diet should become practically a milk diet. Short of this we were unable to prevent scurvy, although the onset of symptoms was delayed and growth of the animal maintained in proportion to the quantity of milk consumed daily."

After considering these observations, it is possible, at least partially, to interpret the apparently divergent results of the various investigators in testing the antiscorbutic properties of cow's milk. In order to make comparative experiments on milk we shall have to take into account the freshness of the product, the diet of the cow, the supplementary value of the milk, and the quantity of milk consumed.[25]

We have considered in more or less detail the importance of milk in the diet, since it is employed so extensively in baby feeding. As we have shown on guinea-pigs and Hess on infants, pasteurized milk is deficient in antiscorbutic vitamins, but there is no reason to doubt that for infants the addition of an antiscorbutic, such as orange juice or

[23] Hart and Steenbock: Jour. Biol. Chem., 1919, 38, p. 267.
[24] Lancet, 1918, 194, p. 1.
[25] Chick and Hume: Jour. Biol. Chem., 1919, 39, p. 200.

tomatoes, may supplement the milk and make an entirely satisfactory ration. From a number of experiments with fresh raw goat milk, the evidence indicates that this is a much more satisfactory food than the Chicago market raw cow milk. Guinea-pigs consuming from 75-85 c c daily of the former with hay ad libitum, gained rapidly and had only evanescent scorbutic symptoms, while those on a daily consumption of from 100-115 c c of raw cow milk had several severe exacerbations. Guinea-pigs given oats, raw cow milk and hay died of scurvy, while the same amount of goat milk, although not entirely preventing the disease, permitted the guinea-pigs to live for over three months.

In a report to be published shortly by Dr. Leila Jackson and myself, we describe the production of mild scorbutic lesions in fetal guinea-pigs when the pregnant mothers are fed on scurvy producing diets. In confirmation of the work of Ingier,[26] it was observed that pregnant pigs on such food were very apt to abort during the first half of pregnancy, in the second half of pregnancy some mothers might give birth to dead or immature fetuses, and others to mature fetuses which on gross examination presented different degrees of mild scurvy. Microscopically, the findings of hemorrhage in the sites so common to hemorrhage in the scurvy of adults was the most constant feature. Occasionally, infractions of the bones with separation of the epiphyses was noted. Hemorrhage in the tooth pulp was almost a constant observation. This apparently could not be due to intrauterine traumatism, but must have had some relation to the disease. The presence of hemorrhage in the tooth pulp also accords with the citation by Zilva and Wells,[27] that scurvy produces marked changes in the tooth pulp.

If after the birth of mature young, the mother is continued on a scurvy producing diet, the nursing young in many instances develop the disease while nursing the mother and gaining weight at the normal rate. The old pig usually dies within two or three weeks, losing weight with extreme rapidity while producing a normal amount of milk as shown by the growth of the young. The young may die of scurvy in a short time, or may recover if placed on a carrot ration. However, in a few experiments, the young, although growing normally while nursing the mother, failed to gain properly when placed on the normal diet. Some of these died within a few weeks, but no gross lesions of scurvy were present.

[26] Jour. Exper. Med., 1915, 21, p. 525.
[27] Proc. Royal Soc., 1919, B., 90, p. 505.

The foregoing observations suggest that when the mother is on a vitamin-free diet, these substances are not supplied by the milk. It would also be suggested that normally the unknown substances are either not manufactured at all by the animal body, or in a very deficient quantity.

There has been and still is, more or less controversy over the relationship of bacteria to diet deficiency diseases. One group holds that these conditions are due to lack of some vital constituent of the food, and the other that bacterial invasion is the etiologic factor. In the microscopic studies of experimental scurvy lesions, Jackson and Moore have described the presence of diplococci in and around hemorrhages. Jackson and Moody[28] have isolated a streptococcus from scorbutic guinea-pigs, and have produced mild lesions by intracardiac inoculations.

Recently Jackson, Pilot and myself had the opportunity to make cultures from the gums and blood of human adult scurvy victims. In one instance an organism of the streptococcus viridans type was isolated from the blood. In all cases the cultures from the crushed gums were practically pure viridans growths. Intracardiac injections of these cultures into young guinea-pigs on a normal diet produced lesions which grossly could not be distinguished from scurvy. However, we found that strains of Streptococcus viridans from other sources produced identical lesions. Injections of certain hemolytic streptococci caused a more severe and somewhat different pathologic picture.

Further experiments are necessary to determine the significance of the presence of bacteria in scorbutic lesions. It is highly probable that some lowering of the resistance due to the one-sided diet permits the invasion of bacteria. Personally, I have considered them secondary invaders, gaining entrance after some breakdown of the natural body defences. If, as some investigators assume, there is increased permeability of the intestinal mucous membrane, we still must be given some plausible explanation for this change.

By way of summary, it must be emphasized that in determining the relative value of such a food as milk for maintenance, reproduction, growth and vitamin content, we must consider several factors. Included in these are the species of the animal employed in the experiments, the freshness and treatment of the milk, the quantity of milk

[28] Jour. Infect. Dis., 1916, 19, p. 511.

consumed, whether alone or with other foods, and the diet and physical condition of the cow producing the milk. Raw and pasteurized Chicago market milk as measured by feeding guinea-pigs were found to be exceedingly poor antiscorbutics. Fresh goat milk had a much higher antiscorbutic value. Certain proprietary infant foods and condensed milks produced severe experimental scurvy.

Experimental scurvy can be produced in fetal guinea-pigs when the pregnant females are fed scurvy inducing diets, such as oats, hay and water, or pasteurized milk and hay. The severity of the disease with the former diet is much greater than with the milk and hay.

The milk from mother guinea-pigs on a scorbutic diet is poor in antiscorbutic vitamins as it does not prevent scurvy in all instances in the nursing young.

Although bacteria are present in the lesions of scurvy, their invasion is apparently not the primary cause of the disease. The cause of scurvy, as far as the present state of our experimental knowledge indicates, is an insufficiency of some substance or substances in the diet which have not yet been isolated.

DISCUSSION

D. J. DAVIS: One point mentioned by Dr. Moore that should be emphasized, is that it is dangerous to carry over results from one variety of animal to another. This has been done, and is being done now, especially by commercial experimenters. They obtain results with certain foods in animals, and then attempt to apply the results to the human being. That, it seems to me, is a wrong thing to do, for food may act differently on man and on animals.

Certain investigators have produced scurvy or scurvy-like symptoms in the fetus of pregnant animals. This is interesting because it may throw light on certain obscure diseases like chondrodystrophy and similar conditions.

Recently considerable work has been done on the relation of vitamin foods to bacterial growth. Apparently, certain bacteria can live and develop on mediums that are free from these substances; that is, they may grow on absolutely pure synthetic mediums. I do not know whether any animal exists that can grow and continue to reproduce on foods that are free from these substances. Perhaps there are such animals, but all animals tested seem to require substances of this sort. It would be interesting to find an animal that can live on absolutely pure synthetic food as some bacteria apparently can. There are certain bacteria, however, especially some of the pathogenic organisms, that apparently require substances of the nature of vitamins. We have known for a long time that small amounts of blood serum or tissue extract added to the medium will enhance the growth of bacteria quite markedly. It has been recently shown by Lloyd in England and Kligler and others in this country that substances of this sort can be isolated from the tissues, and when added in very small quantities to the medium, will enhance the growth of bacteria, especially the cocci.

There is one organism the nutrition of which is rather unique, namely, the influenza bacillus. This organism requires a definite substance—hemoglobin—for its development. Proteids will not suffice; neither will hemoglobin alone. As far as I know, the influenza bacillus is the only form of life of any kind in which such a highly specific substance of definite character is absolutely necessary for its continued existence.

How does hemoglobin behave in the nutrition of these organisms? Does it possibly act like a vitamin substance? The organism requires only a very minute quantity of it—one part in 50,000 is sufficient for growth, and hemoglobin alone is not sufficient. In many other respects this particular body acts like the vitamins do in animals. If it be true that it does act in this way in bacteria, it may throw some light on the way in which vitamins behave in the higher forms.

C. G. GRULEE: Of the vitamin or deficiency diet diseases, the most frequent is scurvy, but the pediatrician sees comparatively little scurvy. It may be that some of the earlier stages of scurvy escape our notice. Hess has reported a sort of epidemic of scurvy in one of the asylums of New York. This epidemic, however, was not scurvy at all as we know it. It seemed to have the preliminary symptoms, some of which, if I remember rightly, were frequency of the pulse and pallor. His findings have never been substantiated by any one else. It may be that the disease was a preliminary stage of scurvy, but so far no other writer has described the condition. Besides this single report of scurvy in a large number of patients, only isolated cases of scurvy appear to have been seen, and in varied conditions. Occasionally it appears in a child fed on the breast; occasionally in a child fed on raw milk. It appears probably more often in children who have been fed milk which has been heated in some way. A report of the American Pediatric Society some years ago was to the effect that most cases appeared in children who were fed on proprietary infant foods, but it seems to me that a criticism of that report can be made, for most children were fed on proprietary food. It has been my custom and probably that of most pediatricians to feed a large proportion of children on boiled milk, and there has been no noticeable increase of scurvy. I have seen two cases of scurvy, as I recall, in the past year. One of these developed in a child who was fed artificially from birth, not on boiled milk, but on a proprietary milk known as Hoos' albumin milk. The child developed scurvy on this food and, of course, promptly recovered on treatment. However, that is only one of many patients whom I have fed on the same food without any special results.

I liked Dr. Moore's last statement, "that it was caused by some deficiency in food about which we know nothing." Though that may not be the exact statement, I take it to be the meaning. I wish that deficiency diseases could be studied from another angle than scurvy. Perhaps there is no branch of medicine in which we see so much of deficiency disease as in the diseases of infants, because we are forced to give the child relatively large amounts of food, most of it chosen from a few articles of diet. One of the chief deficiency diseases is caused by too little food. This became very evident in Denmark during the war, because the people in Denmark were skimming the milk and selling it as butter into Germany. As a result of this one man in Copenhagen saw sixty cases of keratomalacia, which is regarded as a deficiency condition, as a part of marasmus, caused either by too little fat in the food or a diet which is too restricted. We do not know which, but it is supposed to be the result of too little fat in the food. We do know that children who are fed on nonfat food, show a general tendency to and lack of resis-

tance to infection. They become the victims of infection much more easily than children who are able to take a large proportion of fat. This is particularly true of the type of case of which I have spoken.

I hope that a discussion of vitamins in deficiency diseases will not lead the laity or the profession to exaggerate the importance of infantile scurvy. As a mater of fact, infantile scury is not of frequent occurrence and when it does occur, it is amenable to proper treatment.

E. R. LeCount: Many cases of scurvy in adults occurred among the Polish people during the winter two years ago. In the postmortem examinations, one of the things that impressed me was the fact that hemorrhages into the leptomeninges had occurred to such an extent in some cases that it seemed to be the cause of death.

W. E. Post: As to the importance of scurvy, I might say that in the Russian army during one month in the summer of 1917 97,000 new cases occurred. I had an opportunity to see some of the cases, and also to talk to the men who had been working on the problem. The possibility of infection as an element in the etiology of scurvy as it occurred among their soldiers was taken into consideration. It had been reported to the surgeon-general that one physician had maintained himself on a rational diet, had lived and slept in the bed with one of the scurvy patients and had contracted scurvy. The possibility of the transmission of some organism by the louse was a question in the minds of the physicians. No satisfactory conclusion was reached. When we visited Moscow I talked with one of the nurses who had been at the front in Roumania and she said that for two months previous to an outbreak of scurvy in that line those men had nothing to eat but lentil soup.

J. J. Moore: I wish to say in connection with the subject of scurvy in armies that there was an outbreak of scurvy among the English soldiers in Mesopotamia. The Lister Institute arranged for the production of fresh vegetables for the soldiers, and after that the scurvy disappeared. In man there is a long period of latency in scurvy, and it will occur in outbreaks like that in New York described by Hess.

MERCURI-ORGANIC DERIVATIVES

Morris S. Kharasch
Kent Chemical Laboratory, University of Chicago

Oct. 30, 1919

"A new era began with the investigation of medicinal substances by chemists in the early years of the nineteenth century. These researches bore fruit in the isolation of the active principles of many vegetable drugs. The significance of these researches can hardly be overestimated, since it opened up the possibility of accurate study on the effect of dosage and enabled quantitative measurements of the effects of pure drugs to be made."

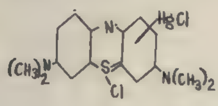
It is held that the physiologic action of a drug is conditioned solely by its physical properties. Even this does not exclude a connection between physiologic action and chemical constitution. No satisfactory theory has as yet been advanced to explain from a single standpoint the therapeutic value of different drugs. As the body is made up of different kinds of cells, each kind with its characteristic properties, it is quite conceivable that a small change in the constitution of a drug may lead to its becoming attached to a different set of cells, thus producing a different physiologic effect. This is essentially Ehrlich's idea. He thought that the selective action of a compound for certain cells depends on the coming together of particular groups in the molecule in some sort of chemical connection with the cell substance. It is only when the compound is held to the tissues by these groups that the whole complex molecule can take effect and exert its characteristic physiologic action.

This "lead" of Ehrlich's led to a series of remarkable researches and culminated in the elaboration of salvarsan. Again Ehrlich also discovered that many dyes are themselves poisonous to certain parasites, and act as chemical specifics in these particular infections.

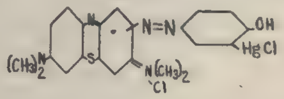
It was observed by Ehrlich that methylene blue had a decided inhibitory effect on tubercle bacilli. In a systematic study of the effect of dyes on the progress of tuberculosis in animals, Dr. Lydia DeWitt of the Sprague Memorial Institute, confirmed Ehrlich's observations concerning methylene blue, first, that it has a high bactericidal power, second, that it penetrates the tubercle and also stains the bacilli. Furthermore, Dr. DeWitt has discovered that methylene blue has

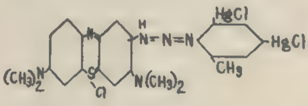
some power to delay the progress of tuberculosis in the animal, and that its toxicity for the animal is very low. Mercury, on the other hand, is known to have a high bacteriotropic power. Its use, however, is limited by its high organotropic power. It seemed reasonable to test the therapeutic effect of methylene blue — mercuric chlorid. This compound had been prepared by Bernthsen, who described it as an amorphous one. It is, however, possible to obtain it in crystalline form. This double salt gave some promising results. The preparation, as such, is very toxic. The toxicity is undoubtedly due to the mercuric chlorid, since all of the mercuric chlorid could be extracted from the compound by merely shaking with ether, although a water solution of the crystalline methylene blue—mercuric chlorid—fails to give a test for mercury when treated with sodium hydroxid or ammonium sulphid in the cold.

The problem then resolved itself into preparing a compound of the following type



in which mercury would be attached to carbon. A close study of the structure of methylene blue and mercury compounds in general revealed the fact that in mercurizing organic compound, mercury would never take the place of the hydrogen which is in the meta position to an amino nitrogen, or any negative group. I might mention in this connection that the attempt to mercurize leukomethylene blue at a high temperature also did not succeed. The idea that next occurred to me was that since it was impossible to mercurize methylene blue directly, we should attach a radicle to it which already contained mercury attached to carbon. Two compounds of the following types were prepared: Methylene blue azo o-phenol mercuric chlorid and methylene blue diazo o-toluidine di mercuric chlorid.

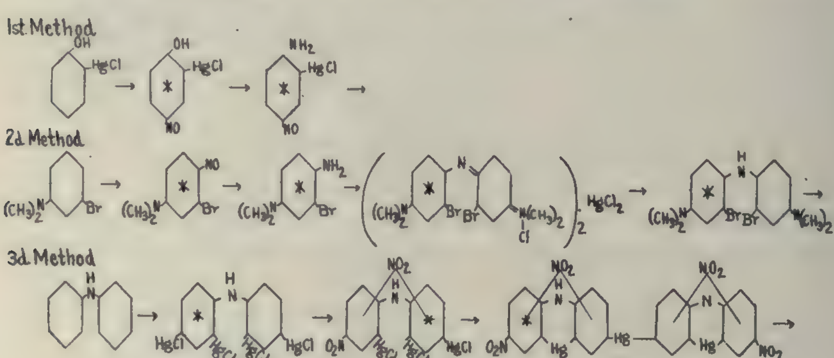




These were obtained by diazotizing in case of the first compound amino-methylene blue and condensing it with o-phenol mercuric chlorid and in the case of the second compound by diazotizing o-toluidin

di-mercuric chlorid and condensing it with methylene blue. The two compounds thus obtained are amorphous and insoluble. It is chiefly due to their insolubility that they have not justified the expectations respecting their therapeutic value.

In the work I have just referred to, our attempts to introduce mercury directly into methylene blue or to attach a radicle containing mercury to methylene blue has not materialized in the sense that the compounds obtained were not of any therapeutic value. We then endeavored to synthesize a methylene blue derivative from compounds containing mercury in the ring, and also to prepare a new type of methylene blue with mercury in the place of sulphur. For this purpose three different methods were employed, all of them being pursued simultaneously. I shall now outline the methods briefly.[1]



DISCUSSION

LYDIA M. DEWITT: As Dr. Kharasch mentioned, this work was begun in connection with my work on the therapy of tuberculosis. I had been interested in methylene blue from the beginning of my work inasmuch as I had worked with this dye in vital staining years before. It seemed as though methylene blue gave as much promise as anything. I found, as Dr. Kharasch did, that it had a very high destructive value for the tubercle bacilli, that about one or two minims would completely inhibit the growth, and that it had the power to penetrate the tubercle in the animal body, and to stain the tubercle bacilli, which is not easy. These facts combined with other considerations indicated that it was worth while to do further work on methylene blue. The chemists, who have been working with me, have been busy for a number of years with the idea of modifying the methylene blue molecule. Many things have been done, such as shown by Dr. Kharasch. We have tried oxygen. We have tried using other things, such as selenium in place of sulphur. We have used mercury attached to

[1] All compounds marked with a * are new and have first been prepared in pursuit of the idea here outlined.

carbon. Mercury is one of the oldest substances used in medicine. Some authors place it back as far as the ninth century. Most of the work has been in connection with syphilis, though mercury has been tried in almost every disease that we know anything about. It has been tried in tuberculosis, but nothing in the way of systematic work has been done. It seemed to me worth while to do something systematic because mercury, as well as methylene blue, has a high inhibitory power over the tubercle bacillus. Mercury in simple combinations has been used for centuries, but the idea that the power of mercury might not be diminished in an organic compound is recent. There are different opinions in regard to the organic preparations which have been given to us. Schamberg, for instance, thinks that the toxicity depends on the percentage of mercury in the body regardless of the size of the molecule. He says this is due to the fact that probably the mercury splits off into a simple mercury salt. If a preparation could be made in which the mercury would be firmly bound to the molecule so that it could not split off, we would have a preparation which would be less toxic and still retain a high curative action. It is along this line that we have been working. The workers on the pathology of mercury and organic mercury salts have found that if treatment is carried on for a certain time, the mercury distributes itself much more rapidly than most of the heavy metals. When it is used for any great length of time we find it in most of the organs, especially in the liver and kidneys. If it is carried far enough, we find it in the lungs and blood. The point of greatest danger is in the kidney, and in order to lessen this danger we have tried to modify the molecule. In my work I have tried a large number of compounds, both simple and complex, inorganic and organic. In all toxic cases so far observed, I suspect that the animals died of mercury rather than of tuberculosis. Of the substances tried, mercury salt of methylene blue has given far more suggestion of beneficial action than anything we have tried. We feel, however, that it is not sufficiently nontoxic, and so we are now working along the line which Dr. Kharasch has explained.

J. STIEGLITZ: That methylene blue has some value medicinally when injected has been indicated by Dr. DeWitt. The structure, which is also the fundamental structure underlying the new class of dyes used by recent British workers, was used experimentally rather extensively during the war. The experiments were so successful that attempts are being made to carry out further work in this country. I want to emphasize the remarkable similarity between methylene blue and acriflavine. The advantage of it, as so far indicated, is that it has bactericidal power.

ON THE QUESTION OF COMMISSURAL NEURONS IN THE AUTONOMIC GANGLIONS

SYDNEY E. JOHNSON
Northwestern University Medical School
October 30, 1919

The question of the origin of the spiral fibers, pericellular networks and intercellular plexuses of autonomic ganglions has given rise to two opposed views. Ehrlich, Retzius, Langley and others believe that they are terminations of cerebrospinal, preganglionic neurons. Some authors (Dogiel, von Lenhossek and others) have, on the other hand, claimed that endings of other types of neurons (commissural, sensory) are also found in these ganglions. The writer has produced experimental evidence in favor of the first view.

Frogs were used for the first set of experiments, as their autonomic ganglion cells are unipolar and the histologic pictures are not confused by the presence of dendrites. Three different lots of frogs were operated.

Results of experiments on the first two lots of frogs were, if considered separately, inconclusive.

Experiments on the third lot gave rather striking results. In these the spinal cord was destroyed and the trunci sympathici cut. This double operation eliminated the possibility (allowing time for degeneration) of preganglionic fibers reaching the posterior ganglions, while preganglionic fibers could reach the anterior ganglions by running from the three anterior spinal nerves caudad or cephalad for some distance in the truncus sympathicus.

In the posterior ganglions all of the spirals and pericellular networks disappeared, while in the anterior ganglions a very few could still be demonstrated.

The evidence thus afforded appears to show: (1) that the spiral and pericellular fibers are of cerebrospinal origin; (2) that these preganglionic fibers may run some distance in the truncus sympathicus before terminating in a network on a postganglionic cell, and (3) that commissural connections do not occur in the autonomic ganglions of the frog.

In a second set of experiments, using cats, both sympathetic trunks were cut well caudad to the lowest white ramus communicans. Allow-

ing from four to six weeks for degeneration, the sacral and coccygeal trunk ganglions were removed and stained by the pyridine-silver technic. In these ganglions the intercellular plexuses have entirely disappeared. No fibers remain which can be interpreted as commissural.

Results of a similar character have been published recently in a series of papers by Professor S. W. Ranson and Dr. P. R. Billingsley. The observations of these authors were mainly on the cervical and thoracic parts of the sympathetic trunks.

THE VITAMIN REQUIREMENT OF YEAST

Roger J. Williams
The Fleischmann Company

October 30, 1919 (Abstract)

The word vitamin was introduced by Casimer Funk. Previous to his time it was thought that the nutritional requirements of human beings could be supplied with proteins, carbohydrates, fats and mineral salts. Funk, however, believed that certain other substances are necessary for human nutrition. The lack of these specific substances in one-sided diets, Funk believed, would cause diseases like beriberi, rickets, scurvy, pellagra and sprue. Funk at one time suggested that even cancer might be due to the lack of a specific substance in the diet. He had experimental evidence in regard to only one of these diseases, beriberi. The substance here concerned seemed to be of a basic or amin nature, and being necessary to life, was called vitamin. The term vitamin was then extended to cover all the hypothetical substances of this nature which he supposed are present in normal diet. The term vitamin has been attacked, particularly by E. V. McCollum, but has been retained for convenience and lack of a better term.

There are now three well recognized specific substances or groups of substances which are necessary in nutrition besides the more ordinary nutrients. One of these substances is the beriberi preventing vitamin, the lack of which causes a form of paralysis in human beings. This disease was first noticed among oriental people who lived almost exclusively on a diet of polished rice. This vitamin occurs in the pericarp of the rice, and the disease does not occur when people eat unpolished rice. The vitamin is widespread in nature, occurring in all common foods, cereals, milk, meat, and so forth. From the first, yeast has been known to be very rich in this vitamin. While it has not been isolated in pure form yet, by means of extraction with alcohol, adsorption on fullers' earth, precipitation with phosphotungstic acid, precipitation with silver nitrate and baryta, and various other procedures, it can be freed from the great bulk of the original material. Many difficulties beset this procedure, chiefly because, while impure, this vitamin is quite stable; when purified, it becomes unstable and may easily lose its properties. R. R. Williams has presented evidence that there is an

isomerism concerned, one isomer being active and another inactive. The vitamin, when pure, he thinks, easily passes over from the active to the inactive form.

There is another substance or class of substances which protects against scurvy. Such foods as fresh vegetables contain the principle which prevents this disease. Orange juice is also potent. Of this so-called vitamin, little is known. Its existence has been doubted, especially by McCollum. McCollum's work indicated that scurvy in guinea-pigs was always accompanied by constipation, and could be cured by mineral oil or artificial orange juice, said to be laxative due to the citrates present. More recent work, however, has practically disproved McCollum's contention. Histologic evidence presented by Hess and Unger has shown that scurvy in guinea-pigs may be, and frequently is, accompanied by constipation, and that mineral oil will remedy the constipation but not the scurvy. Orange juice, on the contrary, will cure the scurvy.

There is a third vitamin, often called the fat soluble vitamin, which is necessary for growth of the young, and the absence of which in the diet of young rats causes disease of the eyes. This vitamin occurs widely in nature, especially associated with some fats, notably butter fat. This vitamin, too, may or may not have relation to the others. The fact is not clear to many that the different vitamins may have no relation to one another. As far as we know, they do not have. We know that they are all necessary in nutrition and that exceedingly minute amounts suffice. This is about all that we know them to have in common.

There may be yet other vitamins, for which experimental evidence so far is lacking. Funk probably holds to his original view that rickets is due to the lack of a specific vitamin. That it is caused by failure to retain calcium, is pretty well recognized. Funk would say that calcium retention is conditioned by the presence of a vitamin, and would point to the efficacy of codliver oil as evidence in favor of his view.

Having refreshed our minds as to what is meant by "vitamin," let us turn to the subject of yeast. This organism has long been studied because of its great commercial importance in the brewery, distillery and bakery.

Pasteur, in his famous researches, found that yeast would grow in a solution of cane sugar, ammonium tartrate and the salts of yeast ash.

Since his day, it has been generally believed that yeast can grow on such a synthetic medium, but that an addition of broken down protein improved such a medium for yeast. Pasteur, however, observed the fact that a particle of yeast the size of a pinhead (containing several million cells) must be used to inoculate such a solution in order to get appreciable growth and fermentation.

In my work I have isolated single cells of yeast in small hanging droplets and made an extensive study of the growth in different media. If single cells are isolated in Pasteur's synthetic solution mentioned, containing ammonium salt as the only source of nitrogen, the majority of the cells will not grow, and those that do grow, grow very slowly and produce ultimately only a few cells. Considering the fact that a single cell in a favorable medium will produce probably 5,000 cells in 24 hours, it is obvious that Pasteur's synthetic solution lacks something important. This lack I have shown quite conclusively to be a vitamin, in fact, the vitamin which in human nutrition prevents beriberi, the vitamin which occurs in yeast and about which most is known. If material containing this vitamin is added to Pasteur's solution, rapid growth takes place from one cell in ratio to the amount of vitamin put in. If a solution such as Pasteur's is inoculated with a fair quantity of yeast, it will grow, owing to the high vitamin content of the yeast added. The evidence that it is actually the beriberi preventing vitamin which the yeast needs, I will omit, as it has been published,[1] and it is a rather long story. Suffice it to say that the substance which prevents beriberi and the substance which promotes yeast growth occur in the same places, have the same properties so far as is known, and no divergent properties.

As there is no reliable chemical test for vitamin, biological tests must be used. There have been in general two methods of testing for this vitamin, either in foodstuffs or during processes of attempted purification. Chickens or pigeons acquire polyneuritis when on an exclusive rice diet for about a month. The material to be tested is then administered, and a more or less complete cure will result if the substance in question contains the vitamin. There are many difficulties in that the fowls often lose their appetite and their trouble may be mainly starvation. Partial cures are not always easily recognized or evaluated.

[1] Jour. Biol. Chem., 1919, 38, p. 465.

Feeding experiments may be carried out also on young rats. If rats continue to grow and do well on a diet, it must contain the necessary vitamin. On the contrary, if a rat does not grow on a diet known to contain everything else necessary, the diet must lack vitamin. This test is, of course, quite reliable, but cannot be used unless a large amount of material is available for an extended experiment. Both of these methods of testing are tedious and long drawn out, but by use of yeast, tests for the vitamin in question can be made easily and quickly. In the course of an hour, 100 or more single cells of yeast can be isolated in media containing the substances in question. After these cells have been incubated for 5 hours, microscopic examination will show qualitatively whether or not vitamin is present. In 18 hours a very good idea of the relative amount of vitamin present can be obtained, as in this time the growth is closely proportional to the amount of vitamin put in. This proportionality holds through quite wide limits. If a very small amount of vitamin material is put in, an average growth of 10 cells results in 18 hours; if the amount of material put in is doubled, the growth is approximately 20 cells, if tripled the growth is approximately 30 cells and so on, even up to 40 times the original amount which will produce approximately 40 times the original growth, or 400 cells in 18 hours. By the use of yeast, the comparative amounts present can be ascertained, and several solutions can be tested in one day. Obviously, this cannot be done in animal feeding experiments. In the use of yeast for this test, extremely small amounts of material are necessary. In one experiment 0.5 mg. of crude material was dissolved in 30 c c of medium with the result that the growth produced by a single cell in 24 hours was increased from 6 to about 70 cells. The amount of crude vitamin-containing material which was in the droplet and actually in contact with the cell was about one two millionth of a milligram.

In addition to the use of yeast as a test for vitamins, it is of interest to know that an organism so far down in the scale of creation has the same vitamin requirement as has the highest organism. The vitamin in question must be a most fundamental nutritional requirement, playing an indispensable rôle in a great variety of organisms. It is possible that a study of its behavior on yeast will throw light on the rôle it plays in other organisms.

If we have a single cell of yeast growing in a medium, the initial rate of growth will be affected very little by doubling or trebling the concentration of sugar, phosphates or ammonium salt. If, however, we double or treble the vitamin content of the medium, as we have seen, we at the same time double or treble the rate of reproduction. This suggests that in human or animal nutrition the vitamin may have an important rôle in the building of new cells. It also suggests that a diet of high vitamin content may be very valuable. The synthetic powers of various animals to form vitamin has often been spoken of loosely. In the case of yeast, it has always been thought that the yeast could manufacture vitamin. As a matter of fact, we do not know for certain where the vitamin does originate. Though it has not been proved definitely, the evidence points to the conclusion that yeast is unable to produce vitamin. If supplied with a small amount of vitamin, the yeast cell will reproduce a few cells, but the rate of production does not increase as time goes on; on the contrary, the growth tends to come to a standstill and further reproduction seems impossible. In case of yeast and its vitamin requirement, the simple rule, "the more the better," seems to apply. It is possible that this rule may also apply to a less degree in human nutrition.

DISCUSSION

F. C. KOCH: I think we have here a method which will probably help to tell us something more definite as to the character of the vitamins, their distribution, and their function. I say that because, in the first place, this is a rapid method. It takes 24 hours to determine the vitamin value of a given material; it is not a question of days and weeks as in the older methods. Secondly, it is distinctly quantitative in character, as pointed out by Dr. Williams. We have confirmed that a number of times and have applied the yeast method in a study of the quantitative distribution of the vitamin element in various organs, and it is an interesting fact that of all the organs we have examined, the hypophysis is the highest in its content of these elements, in that respect apparently confirming some of the work by T. B. Robertson. In the third place, the method is valuable in that it detects very small quantities. In order to make the most progress we must be able eventually to determine the nature of this substance.

D. J. DAVIS: I think it was Loeb who, a number of years ago, pointed out that the mango fly must have yeast, the yeast in his experiments being grown on a synthetic medium. I wonder if that observation has been confirmed

J. STIEGLITZ: I would like to call attention to the series of experiments to which Dr. Koch referred. We are now getting definite evidence about vitamin that is quantitative in character. The question of the effect of heat on the vitamins in milk can be definitely settled. In the second place, I would like to suggest that experiments be made in regard to artificial media of organic

and inorganic material to see whether it really substantiates the present theory. Probably the vitamin is organic, but we ought to have a means of saying definitely yes or no.

J. J. MOORE: I believe Dr. McCollum in a letter has retracted his statements that scurvy is not a deficiency disease. He now admits that there is a scurvy vitamin. It is important to note that Dr. Williams finds the yeast itself unable to make vitamins. It is apparent from animal and human experiments that the body is able to make certain vitamins. We want to find out, and probably will later from such work as that of Dr. Williams, where they come from.

Loeb makes the statement that yeast was grown on a synthetic medium. He did not start, however, with a single cell, as it is impossible to obtain a colony large enough to be visible. I think he was right as to the mango fly. It probably does require the vitamin of yeast for its growth.

In regard to Dr. Stieglitz' question, I think the answer is no. The yeast, of course, contains the principle which will promote growth, but the digestion or destruction of the organic matter destroys the principle.

ANNOUNCEMENTS

At the annual meeting of the Institute, Dec. 1, 1919, L. Hektoen, J. A. Capps, and Dean Lewis were elected governors for five years.

At the annual meeting of the board of governors Thomas L. Gilmer was elected president of the Institute for 1920, and David J. Davis, vice president. L. Hektoen was elected chairman of the board of governors, J. A. Capps, treasurer, and J. Gordon Wilson, secretary.

The following have been elected fellows of the Institute: William D. Haskins, Arno B. Luckhardt, Arthur W. Stillians.

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